













# TEXTBOOK OF MEDICAL TREATMENT

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## PREFACE

THE fifth edition of this book has been subjected to a more complete revision than any of its predecessors owing to the return home from war service of many contributors. All the sections have been thoroughly revised and brought up to date. Some deletions have been made and much new matter added.

Three short new chapters have been included on Antihistamine Drugs, the Treatment of Dehydration and Hypochloræmia and the Care of Old People.

The sections on Infectious Diseases, Penicillin, Venereal Diseases and Diseases of the Nervous System have been re-written by new authors.

The time is no doubt ripe for all doses to be expressed in the metric system, and in the case of the newer drugs such as the organic arsenicals, the sulphonamides, folic acid, B.A.L., etc., this system has been invariably adopted. Most practitioners, however, are accustomed to the apothecaries' system of doses in the case of the older drugs. It was felt, in consequence, that any attempt to express the dosage of these latter in the metric system, however desirable it might be to do so, would result in much bewilderment. While, therefore, we have continued to use the older system for the galenicals, an approximate metric equivalent has been included in brackets after each dose in the hope that this may encourage the more widespread use of the metric system and make the book more intelligible to readers in other countries where that system is in vogue.

Much confusion is caused in practice by the perplexing variety of names given by manufacturing chemists to their proprietary preparations. In this book the pharmacopœial or official name for a drug has been invariably used when this is available. A table showing the proprietary equivalents of the official preparations mentioned is given at the end of the book. We are much indebted to Mr. W. Mair, F.R.S.E., F.C.S., M.P.S., for his very thorough and painstaking revision of this list.

We are grateful to many correspondents who have drawn our attention to errors of omission or commission in past editions.

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## PREFACE

THIS book has been written for students and practitioners in the hope that it may fill the therapeutic gap left by the majority of textbooks on general medicine in which, owing to exigencies of space, the section devoted to treatment is often inadequate. In addition, the information given is not infrequently couched in such indefinite terms as to be of little value in helping the practitioner to determine whether a particular line of treatment is worthy of trial and, if so, how it can be put into practice. The following statements, for instance, are frequently made: "vaccines may be of value," "arsenic may be tried," "a well-balanced diet should be given," "the general health should receive attention." Further, it is not uncommon for many drugs and measures recommended by our forefathers to continue to be included in such works year after year in spite of the fact that some of them have been shown to be useless and others are known to be less efficacious than modern substitutes.

An attempt has therefore been made by the authors of this book to be extremely explicit in regard to the treatment recommended, in the hope that the directions given will suffice to enable a doctor without much previous experience to carry out the measures which have been described. As far as possible the indications, contraindications and dangers of each recommended method or drug are fully discussed.

Further, an attempt has been made to indicate why and when certain drugs and methods formerly widely used should no longer be employed for the particular purpose under discussion. From this it follows that the number of drugs advised are considerably fewer than in some books of therapeutics, but this we believe to be wise, for undue reliance on the "bottle of medicine" has tended in the past to obscure and diminish the importance of certain general measures of paramount importance which may be included under the heading "General Management of the Patient," i.e., diet, rest, exercise, nursing, etc., which in the past have received too little attention in medical teaching and textbooks. In addition, the general problem of handling patients and relations under the various circumstances which continually confront the young doctor is dealt with. This entails a consideration of what information should or should not be given to the relatives and patient in certain circumstances, and general advice on where and when to send patients to sanatoria, spas or for a change of air and climate. Lastly, the good management of a case frequently requires a knowledge of common-sense psychological principles which are so important in the art of medicine.

It is well recognized that in some diseases where no specific therapy exists a variety of methods of treatment may be advocated by different authorities. In others, even though the general principles of treatment are unanimously approved, yet the details of their practical application may vary widely in different hands. For example, it would be generally admitted that a case of severe diabetes requires insulin, but opinion differs upon the

type of insulin to be used, the details of its administration, and upon the quantity of carbohydrate to be allowed in the diet. No attempt has been made in this book to give a comprehensive description of all the possible methods of treatment which have been recognized to be of value. To do so would greatly increase the size of the book and would, in addition, defeat the object aimed at, namely, to present to the student and general practitioner the subject of medical therapeutics in a simple and rational form. Accordingly the authors have selected for description those methods which from their personal experience they have found to be most useful. When the procedures are of such a specialized nature as to be outside the scope of the general practitioner, only a brief outline is given.

The work is not a small handbook of treatment, nor yet a vast encyclopædia, since there are already a number of such books. Neither is it a textbook of pharmacology, since a large portion of the book deals not with drugs but with the "Management of the Case" in the widest sense of the term. It is not concerned with surgery, but includes sections on the treatment of venereal diseases, tropical medicine, some diseases peculiar to infants, common diseases of the skin, industrial diseases and the neuroses. There is, in addition, a section which describes in detail the technique of certain essential medical procedures—such as lumbar puncture, venesection, paracentesis, blood transfusion, oxygen therapy, etc.

It is a pleasure to acknowledge the help received from Mr T. H. Graham and Miss Margaret P. Russell, M.A.—Librarian and Assistant Librarian in the Royal College of Physicians, Edinburgh—for their help in proof-reading and in the compilation of the index; to various editors and publishers who have given us permission to use certain plates and diagrams appearing in their journals, and in particular to Messrs Lippincott, of Philadelphia, the publishers of "Body Mechanics," and to Messrs Oliver & Boyd, publishers of the *Edinburgh Medical Journal*; and, lastly, to Mr McDonald Walker, of Messrs E. & S. Livingstone, who on all occasions has assisted us in every possible way.

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# INFECTIOUS DISEASES

## INTRODUCTION

**I**NFECTIOUS diseases result from the successful attack upon the tissues of man by pathogenic micro-organisms. In order to treat them successfully it is essential to understand how the organism achieves its success; for a knowledge of its mode of attack will enable us not only to plan the immediate treatment more satisfactorily but also to foresee the kind of complications which are likely to arise and thus be more prepared to cope with them.

It is essential at the outset to make a distinction between bacterial and viral diseases. In the former, the organism remains mainly extracellular and can thus be reached with comparative ease by substances which are present in the blood stream. Although it is reasonable to assume that there is a temporary stage of viræmia in many of the virus diseases, the causative organism is only capable of growth inside the body cell and thus becomes rapidly inaccessible to the usual methods of treatment. Such localization of the virus in body cells has largely occurred by the time the infection becomes manifest and, up to the present, no method has been devised of modifying the effect after the cell has been parasitized. The specific treatment of virus diseases therefore still remains beyond our reach. It must be remembered, however, that the effect of this cellular damage is to open up pathways for bacterial invasion so that many of the virus diseases are followed by complications of a bacterial nature. These secondary complications may sometimes be averted by the use of antibacterial measures, but when not so averted the same measures are usually effective in their treatment.

An acute infection may, then, be regarded as a struggle between a susceptible host and a pathogenic organism. Successful treatment resolves itself into measures designed both to increase the resistance of the host and to diminish the attacking powers of the bacterium. The former, which comprise the management of the fever case, will be dealt with in the succeeding section. To some extent, their importance has lessened as the use of antibacterial measures has shortened the febrile period of most of the diseases; but they remain of importance, for in the severe case of infection it is still true to say that proper supportive medical and nursing measures are necessary for success in its treatment.

Attack upon bacterial infection can be achieved by two different methods.

**Serotherapy.**—Immune sera, human or animal, depend for their effect upon the presence of specific antibodies. There are two types, antibacterial and antitoxic. The former have not proved effective in the treatment of human disease and their use is not advised. Although the latter have found a real place in treatment, their limitations must be fully appreciated. In the first place they are really agents conferring a passive immunity. In other words, they will combine with any free toxin present and protect the host against further production; but will be unable to dislodge toxin

which has become fixed to the body cells. The effect is therefore in no way retrospective; no dose, however large, can compensate for tardy administration. Further, the initial dose must be large enough to neutralize all of the toxin actually free at the time of its administration, so that repeated dosage must be regarded as unsatisfactory. Finally, since time is thus an important factor, the method of administration is important. It is not sufficiently realized that a considerable period elapses after subcutaneous or intramuscular injection of serum before maximum levels are attained in the patient's blood. In some cases this may be as long as thirty-six or forty-eight hours—a dangerously long time. When the patient is regarded as severely toxic, therefore, *serum must always be given by the intravenous route.*

**Chemotherapy.**—The use of the sulphonamides and of penicillin forms the basis of much of the modern treatment of the infections and the reader is referred to the appropriate sections for a full review. Since these methods of treatment are specifically antibacterial, a close link between the practitioner and the bacteriologist is essential. Too often, apparent failures of treatment are found, on investigation, to be due to the presence of an organism which was not susceptible to chemotherapy. Bacteriological investigation gives more precise information before treatment is started than after.

### GENERAL MANAGEMENT OF THE FEVERED PERSON

Fever may be regarded as a reaction of the tissues to invasion by micro-organisms and their toxins. Although pyrexia, arising from interference with the function of the heat regulating centre, is a cardinal sign of fever, in some cases, and those the most toxic, the temperature may not be raised above normal. Wasting, due to increased catabolism; dry hot skin, acceleration of the pulse and respiration; coated tongue, anorexia, vomiting and constipation or diarrhoea; headache, restlessness, insomnia and delirium; and quantitative and qualitative changes in the urine; all these manifestations of fever are a result of the reactions of the tissues of the host to the action of the bacterium or its products.

The primary essentials in the general management of the fevered person are (a) rest; (b) skilled nursing; (c) fresh air; (d) a suitable diet with adequate intake of water; and (e) relief of symptoms.

**Rest.**—Confinement to bed is essential as long as the temperature remains elevated, and should be continued for a varying period in convalescence. A strictly recumbent position should be enforced in those diseases characterized by a marked toxic action on the cardio-vascular system, for damage is peripheral as well as myocardial.

A single bed and firm mattress are preferable for nursing purposes. Careful bed-making greatly assists the patient's comfort. A rubber mackintosh across the bed covered by a taut drawsheet will prevent extensive soiling and save linen. The bed should be made twice daily—oftener if the patient is perspiring profusely. An adequate supply of pillows will make for a more comfortable decubitus. Bedclothes should be light and not tucked in tightly: a cage at the foot is often desirable.

Quietness in the sickroom and its environment is essential. Although a sickroom with a sunny exposure is to be preferred, during the acute stage of the more serious infections, sunshine may be sacrificed for freedom from noise. Traffic in and out of a sickroom should be cut down to a minimum,

and attendants should wear soft-soled shoes. Mental rest is of great importance. Measures should be taken to allay worry and anxiety. Business matters and domestic problems should be shelved until the patient is fit to cope with them. Visitors should be limited to near relatives, whose stay should be brief.

The ideal sickroom is airy, bright and well-ventilated, heated by an open coal fire. Proximity to a bathroom, which should if possible be reserved for the patient's use, is advantageous. An upper floor is usually quieter and more removed from household activities. The temperature of the sickroom should be kept around 55° F. except in the case of infants or the aged, when it may with advantage be raised to between 60° and 65° F.

The bed must be so placed that the patient is readily accessible from both sides, out of direct draught, and not facing a window or other source of bright light.

Furniture, hangings and carpets should be reduced to a minimum, and those retained of such a type as to permit of subsequent disinfection if considered necessary.

A prominent warning notice on the door of the sickroom will serve the same purpose as the time-honoured sheet moistened with disinfectant. The risk of aerial conveyance of infection from the sickroom is negligible.

**Nursing.**—The value of skilled nursing in fevers is generally recognized, but, unfortunately, the ideal of a fever-trained nurse for every infectious patient is as yet unattainable.

Broadly speaking, the notifiable infectious diseases should not be treated at home unless trained nurses can be provided. The non-notifiable infections, such as measles and whooping-cough, present a special problem. Young children suffering from these diseases require skilled nursing care, but, owing to lack of hospital accommodation, must of necessity be treated at home. In most cases, providing the child is looked after by a sensible mother or near relative who can be relied upon to carry out conscientiously the detailed instructions given by the physician, progress will be satisfactory. If the attendant has not already suffered from the particular disease, the risk of contracting infection should be pointed out, and advice must be given as to how the risk of personal infection and the conveyance of infection to other members of the family may be minimized. Overalls, kept in the sickroom, should be provided for the use of the attendant and physician, and a bowl containing a solution of perchloride of mercury, lysol or dettol (chloroxylenol) should be available for disinfection of the attendant's hands.

Although it is not within the scope of a book of this type to describe minute details of nursing technique, one or two points about which the practitioner may be called upon to instruct the unskilled attendant should be emphasized.

The *skin* should be kept clean by sponging with soap and warm water daily, especial care being paid to areas liable to soiling. These should be freely dusted with talcum powder. The body should be washed and dried limb by limb and the windows kept closed during the process. Frequent massage of pressure areas with spirit must always be advised; the seriously ill patient must have his position changed every four to six hours.

**Food** should be given at strictly regular intervals and should be removed from the sickroom between meals; food remains should be burnt. Cold water must be given without stint and be offered at frequent intervals. In

young children the *mouth* should be gently cleansed after each meal by inserting the index finger enveloped in cotton-wool soaked in warm water or warm solution of bicarbonate of soda containing 30 gr. (1.8 gm.) to 1 pint. In older children the teeth should be brushed and the mouth rinsed with warm water or mild antiseptic solution. The lips may be smeared with vaseline or boracic ointment.

*Nasal discharge* must be promptly removed on rags or paper handkerchiefs, and the nostrils gently cleaned with a cotton-wool swab soaked in warm normal saline or bicarbonate solution. Older children should be encouraged to clear the nose by gentle blowing. Vaseline or boracic ointment applied to the nostrils and upper lips will prevent crusting and excoriation.

The *eyes* may require regular cleansing and saline swabbing is usually best. In adults care should be taken during long periods of toxæmia that the eyes are closed periodically. A drop of castor oil on to the cornea morning and evening may prevent a nasty ulceration.

A proper *temperature chart* should always be kept. In young children the temperature should be taken by inserting the clinical thermometer into the rectum, groin or axilla, and not into the mouth. Charting of the pulse is as important as the temperature; merely writing down the figures does not convey the same information as a chart.

All *excreta* should be removed from the sickroom and consigned to the closet as quickly as possible. Care must be taken to avoid contamination of water-closet seats. Specimens required for the physician's inspection should be placed in covered fly-proof receptacles. Articles soiled with excreta must be disinfected. Swabs used for wiping away discharges from the mouth, nose, ears, eyes and other organs must be burnt.

Food should be protected from flies. In summer, spraying of the sickroom with D.D.T. will usually prove effective in eradicating flies altogether.

**Fresh Air.**—Free ventilation of the sickroom is essential. Apart from the diminished concentration of bacteria in the atmosphere, the free movement of cool air has a very important tonic influence on the patient. The appetite and circulation improve, the patient is less restless and sleeps better. In equable weather treatment in the open air is the ideal, failing this the bed should be moved close to a widely opened window. The patient must be kept warm by extra hot bottles and blankets if necessary, and sheltered from strong winds and excessive sunlight. Caution must be exercised in exposing young infants and the aged to open-air conditions.

**Diet.**—The characteristic change in the metabolism of fever is the greatly increased destruction of the nitrogenous-containing tissues of the body. Instead of endeavouring to make good this loss by an increased nitrogenous intake it is a better policy to supply an abundance of "protein spacers" in the form of carbohydrates. Fever patients strongly dislike fatty foods. On theoretical grounds a high caloric intake is indicated, but in actual practice, owing to loss of appetite and actual distaste for food, this is impossible to attain during the height of the fever. Although the semi-starvation diet favoured by Hippocrates, who fed his fever patients on thin barley gruel and wine, may be appropriate in fever of a few days' duration, there can be no question that in more prolonged fevers the patient should be fed up to the limit of his digestive capacity. The absorption of light articles of diet is almost as perfect in the febrile person as in health.

In drawing up a diet it is essential that the likes and dislikes of the patient should be studied and no article for which the patient expresses a strong predilection withheld unless there is a good reason for doing so. Sudden changes in diet are better avoided.

When the febrile period does not exceed four or five days, the diet should be restricted to fluids and "feeding up" is to be deprecated. One and a half to three pints of milk daily usually form the basis of the diet. Not more than 5 to 6 oz. should be given at a feed. The milk may be boiled, diluted, citrated, peptonized, treated with lactic acid, or flavoured with tea or coffee according to circumstances. Whether administered hot or cold is a matter of taste. Glucose is a most valuable and easily assimilated food, which should be given freely in the form of sweetened lemon or orange juice drinks. From 5 to 10 oz. of glucose can readily be administered in the twenty-four hours. Cane sugar is not a satisfactory substitute. Albumen water, jellies, clear soups, eggs and custards are useful additions to the diet and varying flavouring agents can add spice to an otherwise monotonous round. Because of their low nutritive value, high content of extractives, and relative cost, the various commercial beef-juce preparations have little to commend them. Feeds should be given at two-hourly intervals during the day and every four hours during the night if the patient is awake.

The free intake of water favours the elimination of toxins. Hence the patient should be encouraged to drink cold or hot water freely between feeds. Including glucose lemonade, the water intake should amount to at least 4 pints in the twenty-four hours; the greater the consumption of water the better.

Alcohol should not be administered as a routine except to alcoholics or elderly patients, to whom  $\frac{1}{2}$  oz. of whisky diluted with twice its volume of water may be given at two to four-hourly intervals.

When the febrile period exceeds one week the above diet will require to be supplemented on the lines described in the section on the Treatment of Enteric Fever.

**Relief of Symptoms.**—A drug should only be prescribed when there are definite indications for its use, and should be administered in draught or powder form, not in tablets. Unless otherwise stated, the doses prescribed in this section are for administration to adult patients.

**Pyrexia.**—A raised body temperature is in itself not harmful. Indeed, the presence of fever is a natural reaction to infection and attempts to reduce it by drugs are undesirable. In mild cases of fever the following simple diaphoretic mixture may be administered every four hours:—

R	Pot. Cit.	.	.	.	.	gr. 20 (1.2 gm.)
	Liq. Ammon. Acet. Dil.	.	.	.	.	fl. dr. 2 (7.2 c.c.)
	Syr. Aurant.	.	.	.	.	fl. dr. 1 (3.6 c.c.)
	Aq.	.	.	.	ad	fl. oz. $\frac{1}{2}$ (14.2 c.c.)

When the temperature exceeds 103° F., the skin of the whole body should be sponged with warm (98° F.), tepid (80° F.), or even cold water. Quite apart from any effect in reducing temperature, the application of tepid or cold water to the skin exerts an important reflex tonic effect on the nervous, respiratory and circulatory systems, and is very refreshing for the patient. This is particularly important at night, and a tepid sponge-down will often soothe a restless patient and permit a period of good sleep.

Hyperpyrexia (106° F. or over) can sometimes be controlled by the cold pack, rubbing the skin with ice or by the cold bath. The application of the cold pack consists of wrapping a sheet wrung out of cold or iced water around the patient. The cold-bath treatment is difficult to apply in general practice, and, in fact, is rarely necessary. The patient should be immersed in water at 85° F., which is then gradually cooled by the addition of ice or cold water. During the application of any of these procedures, ice or cold water should be applied to the head, the condition of the patient carefully watched, and the treatment stopped when the temperature has fallen to 102° F. The appearance of hyperpyrexia is always alarming, for it must be appreciated that it is often impossible to effect any remission of temperature by these methods of treatment.

Drugs such as amidopyrin, phenacetin, aspirin, etc., should not be prescribed for the reduction of temperature.

*Headache and Malaise.*—A combination of 10 gr. (0.6 gm.) of acetylsalicylic acid and  $\frac{1}{4}$  gr. (16 mg.) of codeine administered at intervals of six hours usually gives relief. Should headache persist, phenacetin, caffeine and phenazone—3 gr. (0.18 gm.) of each—may be prescribed in place of the above; the powder to be repeated every two hours for three or four doses. Diminution of intracranial pressure by lumbar puncture affords immediate relief in infections of the central nervous system. In the most intractable cases a hypodermic injection of  $\frac{1}{4}$  gr. (16 mg.) of morphine will be necessary. When headache is severe a quiet environment and the exclusion of bright light add to the comfort of the patient. A prolonged hot bath is very soothing for general aches and pains.

*Insomnia and Delirium.*—Restlessness and inability to sleep are characteristic symptoms in febrile cases and should always be taken seriously. Nursing technique should first be reviewed and everything done to make the patient comfortable. Where sleeplessness is due to worry or anxiety, a hot toddy with 15 gr. (0.9 gm.) of chloral hydrate is frequently successful. The relief of headache may cure the insomnia. If pain is keeping the patient awake, then either 15 gr. (0.9 gm.) of Pulv. Ipecac. et Opii or 15 minims (0.9 c.c.) of tincture of opium should be prescribed; relief may only be obtained by the hypodermic injection of  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. (11 to 16 mg.) of morphine.

Two drachms (7 c.c.) of paraldehyde is another excellent and safe hypnotic; unfortunately it has a most unpleasant taste and odour. It may be administered by mouth well diluted with whisky or brandy and water, or by the rectum, 4 drachms (14 c.c.) in 4 oz. of starch mucilage. Barbitone or soluble barbitone, in a dose of  $7\frac{1}{2}$  gr. (0.45 gm.) and butobarbital,  $1\frac{1}{2}$  gr. (0.09 gm.), are valuable for their general sedative as well as their hypnotic effect.

Once a sleeping draught has been prescribed it is essential to see that the desired result is attained. This may necessitate repetition of half the initial dose at hourly intervals up to the limit of safety for the particular drug employed. Detailed written instructions regarding dosage should be given to the attendant.

Mild confusion can usually be controlled by chloral and bromide, but active delirium calls for the hypodermic injection of  $\frac{1}{4}$  gr. (16 mg.) of morphine with, in cases of maniacal excitement, the addition of  $\frac{1}{100}$  gr. (0.6 mg.) of hyoscine hydrobromide; the injection may be repeated after an interval of one hour. It should be again repeated that remaking the bed, rearranging the patient's position and a tepid sponge-down will often induce a refreshing sleep.

*Nausea and Vomiting.*—Common initial symptoms in many febrile conditions, nausea and vomiting are rarely sufficiently severe or persistent to call for active treatment. In the majority of cases the symptoms will rapidly subside as soon as specific therapy brings the infection under control. If nausea continues, fragments of ice may be sucked, and a powder consisting of sodium bicarbonate and bismuth oxycarbonate—of each gr. 10 (0.6 gm.)—administered four-hourly, stirred in a little water.

Persistent vomiting should be treated by the intravenous infusion of 5 per cent. glucose saline. Where circumstances do not permit of this procedure, 5 per cent. glucose saline may be administered four-hourly by the rectum. The hourly administration by mouth of 1 minim of tincture of iodine in a teaspoonful of water for eight doses is sometimes a helpful procedure.

*Constipation.*—In most infections, constipation is present. The only satisfactory method of emptying the bowel, and it is usually desirable to do so, is by the administration of a bowel wash-out. Soap and water or warm saline may be used and should be run in by means of a catheter and funnel. A Higginson's syringe should never be used. After the fluid has run in, if soap and water is used, the patient should be placed on a bed-pan; if saline has been used the fluid contents may be syphoned off into a receiver at the side of the bed—usually better if the patient is extremely toxic. Either of these procedures is much less exhausting to the patient, and more sure in its action, than the administration of purgatives. Should constipation be a feature of the illness, as for example in enteric fever, the bowel should be washed out every second day.

In convalescence from a severe fever the bowel habit has to be regained. Liquid paraffin is useful and may be given in 2-drachm doses every four hours during the day. The use of aperients should be a matter of discussion with the nurse; the doctor should not allow the nurse full control of this aspect of treatment.

## DISINFECTION

The aim of disinfection is to destroy the germs which are cast off from the patient in the various excretions. Objects with which the patient comes into contact are liable to be contaminated with pathogenic organisms, particularly clothing and utensils, and may remain a potential source of infection to others for a varying period of time.

The daily disinfection carried out in the sickroom is termed "current" disinfection. The disinfection of the sickroom after removal of the patient to hospital, or after recovery, is termed "terminal" disinfection. The more efficiently "current" disinfection is performed the less need will there be for an elaborate disinfecting ritual after recovery.

### CURRENT DISINFECTION

The aim of current disinfection is the prevention of spread of bacteria from the patient to his surroundings. If steps are not taken to limit such spread then the numbers of organisms will increase in the sickroom and the air and dust will become charged with infective material. The attack on germs may be focussed upon three main sources of infection.



**The Patient.**—All discharges emanating from the patient must be assumed to be infective. Attention should be particularly directed to—

*The Respiratory Tract.*—Coughing and sneezing should be guarded by the use of gauze handkerchiefs. Sputum, nasal, aural or ocular discharges should be carefully collected in clean gauze or paper handkerchiefs and placed in paper bags to be burnt.

*Alimentary Tract.*—Vomitus should be collected in a basin and disinfected. If the linen is soiled it should be steeped in disinfectant and then washed. In nursing children, vomiting often occurs unexpectedly and the bed linen may be saved by the use of towels and old sheets at the top of the bed or cot. Fæces and fæces-soiled bed linen must be promptly disinfected.

*Discharges from Wounds, Abscesses, etc.*—Strict asepsis is of course essential in attention to all wounds. Steps should be taken to avoid soiling of pillows and bed linen with discharge, for as this dries it may be shaken off to join the dust of the room. All fluids removed for testing (blood, cerebrospinal fluid) must be disposed of carefully.

**Articles closely associated with the Patient.**—The most important of these are the bedclothes, linen, towels, etc. All of them become heavily contaminated, and if the bed is made vigorously, organisms will be liberated into the air of the room. The enclosing of the blankets in linen sheets will tend to limit the amount of “fluff” disseminated when beds are made. The nurse should be trained to avoid vigorous movement of bedclothes, mattresses, etc. Feeding utensils are best kept separately for the patient. After each meal the dishes should be washed and scalded by pouring a kettleful of boiling water over them. Toys and comic papers are a dangerous source of transfer in the case of children. It is best to use playthings which can be burnt.

**Articles less closely associated with the Patient.**—Here the first matter of importance is the training of the attendant to observe certain rules. The hands will become grossly contaminated by bed-manipulations, cleansing of discharges, etc., and the nurse must learn always to wash and disinfect the hands after any attention to the patient. An overall or gown should be worn as soon as the sickroom is entered and removed before leaving. The fact that the air and dust of the room is charged with infection should be explained. Damp-dusting, wet-mopping of floor surrounds and the avoidance of “brush-and-pan” should be insisted on. Vacuum cleaners are useful—but very noisy for the ill patient. When they are used, it must be remembered that the contents of the bag are heavily infected and that it should therefore be emptied with care.

The attendant must in this way be “inoculated” with the concept that the patient is the centre of a series of concentric circles; infection is most dense at the inner circle and the constant endeavour must be to prevent spread outwards. The air and dust of the room form one of the important pathways whereby the outer circles become contaminated, so that all steps to reduce dust and the careless circulation of air which disturbs dust will tend to limit spread. These measures are not only of importance in preventing the infection of others; the patient himself, especially if nursed alongside other patients, may acquire secondary complications from the implantation (particularly in the respiratory tract) of organisms acquired from infected dust.

The use of a mask by the attendant is optional; only when the patient is under the age of a year should it be insisted on; for at this period of life a very ill infant may have its chances of recovery reduced by the acquisition of secondary infection. The wearing of a mask is particularly desirable when the baby is being bottle-fed. To be effective, a mask must be of the thickness of at least six to eight folds of fine gauze.

### TERMINAL DISINFECTION

After the common infectious diseases less importance is now attached to the terminal disinfection of the sickroom. It is now realized that the patient is the real danger and that there is little risk of infection arising from contamination of the walls, floor or furnishings of the sickroom. Viruses (smallpox excepted) appear to lose their infecting power very rapidly after leaving the human body.

**Domestic Cleansing.**—Provided current disinfection is conscientiously practised throughout the course of the illness, a *thorough* domestic cleansing is all the terminal disinfection that is required in the majority of the infectious diseases dealt with in this section. Bed and body linen should be treated in the manner already described. The mattress, outer garments, carpets, etc., should be exposed to fresh air and sunlight for a day or two; carpets should be run over with a vacuum cleaner. The room and furniture should be washed with soap and warm water. After thorough ventilation for twenty-four hours, the room may be put in order for the next occupant.

**Formalin Spray.**—The elaborate disinfecting procedure necessary after the removal of a case of smallpox is carried out by the local Public Health Department and includes such measures as the steam disinfection of all bedding and clothing, the spraying of the room with formalin, 8 oz. to the gallon of water, followed by closure for six hours, and the stripping and washing down of walls.

In typhus fever special measures have to be taken to destroy lice (see p. 278).

The reader is referred to textbooks on Hygiene for details of these procedures.

## ANTHRAX

Anthrax is a gastro-intestinal infection which affects horses, cattle, sheep and goats. The disease is conveyed to man through contact with infected animals or with skins and hides, wool, hair or bristles which are contaminated with secretions containing the spores of the anthrax bacillus. The disease is essentially an occupational risk, and in man is more or less confined to workers with animals or in wool, hair or hides. Infected shaving brushes have in the past been responsible for the conveyance of anthrax infection in several instances.

Infection usually enters through minute wounds or abrasions on the exposed skin, giving rise after an incubation period of about twenty-four to thirty-six hours to a cutaneous lesion, the "malignant pustule." Early diagnosis of the lesion, by enabling prompt treatment, greatly improves the prognosis. The spores are occasionally ingested or inhaled, giving rise to the gastro-intestinal or pulmonary forms of the disease, which are almost invariably fatal within three to four days.

Anthrax is not a notifiable disease, but information regarding cases

occurring in factories and workshops must be forwarded to the Chief Inspector of Factories at the Home Office.

**Preventive Treatment.**—Various legal enactments dealing with the disposal of anthrax-infected animal carcasses, the disinfection of infected cattle sheds, etc., the disinfection of wool and hair imported from Asia and Egypt, and the prohibition of importation of Japanese shaving brushes, have played an important part in diminishing the incidence of the disease in this country.

Special preventive measures are enforced in factories, including the provision of exhaust ventilation, the wearing of overalls, the provision of ample washing accommodation, etc. Workers with skin lesions are excluded.

So far as the individual is concerned great care must be taken in handling infected material. Rubber gloves should be worn and are essential if there are any abrasions on the hands. Nurses or attendants must handle infective discharges from the "pustule" or the respiratory and intestinal tracts with great care. Contaminated dressings should be promptly burnt and discharges disinfected. Bedclothes, mattresses and bed linen must be thoroughly disinfected or preferably burnt.

**Curative Treatment.**—*Serum Treatment.*—Early injection of Sclavo's anti-anthrax serum was previously an effective treatment for the cutaneous form of the disease. An initial intravenous injection of 100 to 200 c.c. of serum was followed by a daily intravenous or intramuscular dose of 100 c.c. until improvement ensued.

*Arsenical Compounds.*—If serum is not available, 0.6 to 0.9 gm. of neo-arsphenamine should be administered intravenously and the injection repeated on the following day. In exceptionally severe cases a third injection may be given on the fourth day. One injection of arsphenamine appears to be sufficient to effect a cure in some cases. The best results appear to be obtained when serum treatment is supplemented by arsenical administration. Neokharsivan, together with serum, is administered intravenously by tube and funnel, 0.3 mg., 0.45 mg. and 0.3 mg. on the first, third and fifth day of treatment.

*Sulphonamides and Penicillin.*—Sulphonamide alone is inadvisable, but when sulphadiazine is combined with serum the local oedema seems to diminish more rapidly. The susceptibility of *B. anthracis* to the action of penicillin suggests that a combination of local and systemic administration will constitute a satisfactory method of treatment. A dressing of penicillin cream (0.5 mega units per gram) should be used and 0.5 mega units per day given systemically.

At present we would consider the treatment of choice to be a combination of penicillin and arsenic as described above.

*Treatment of the Lesion.*—As excellent results follow purely medical treatment, the local lesion should not be excised. Immobilization of the affected area either by sandbags or splints is essential.

*General Management.*—Owing to the ever-present risk of septicæmia it is wise to confine the patient to bed even if there is no fever.

When constitutional disturbance is present the case should be treated on the lines indicated for any acute febrile condition, and preferably in the open air.

Vomiting, diarrhoea, headache, delirium, convulsions and cardio-vascular failure, common manifestations in septicæmic attacks, require appropriate symptomatic treatment.

## CEREBROSPINAL FEVER

*(Epidemic Cerebrospinal Meningitis—Spotted Fever)*

It is now clear that acute meningeal involvement must be regarded as only one form of meningococcal infection. Two other syndromes—acute fulminating septicæmia with adrenal hæmorrhage and chronic septicæmia usually unaccompanied by meningitis—are especially likely to be seen during epidemic periods; indeed, the practitioner should have them especially in mind during the first two months of the year when the annual prevalence is at its height. For the recognition of both, the first essential is that the clinician remembers the possibility of their occurrence; the features are sufficiently definite to permit a clinical diagnosis with a fair degree of accuracy. The attention of the practitioner is drawn to their existence, for in one—chronic septicæmia—correct treatment achieves rapid cure and may, in some cases, prevent subsequent meningitis; while, in the other, only the most rapid diagnosis and immediate institution of proper measures hold out any possibility of recovery. The whole course from onset to death of a case of acute septicæmia with suprarenal hæmorrhage may take but a few hours. In many fulminant cases of meningitis, too, the extensive nature of the skin hæmorrhages suggests the possibility of suprarenal damage; these cases should receive the appropriate treatment about to be described.

The other reason for reminding ourselves of their existence is that they draw attention to the mode of access of the meningococcus to the meninges. This route is—nasopharynx, blood stream, choroid plexus, meninges. Every case of meningococcal meningitis should be regarded as bacteriæmic. Treatment must thus be aimed not solely at the meninges but also at a systemic infection. It is perhaps because the sulphonamides can follow so closely the route of the meningococcus that they have proved more efficacious than penicillin.

Cerebrospinal fever is a notifiable disease.

**Prevention and Epidemiological Control.**—There is little doubt that carriers play an important part in the spread of the disease, and because of this it used to be regarded as valuable to search for carriers on the occurrence of a case. It is now appreciated that a simple routine examination of the nasopharynx on a single occasion may well fail to isolate the organism; although repeated examinations will often succeed. This is especially the case in closed or semi-closed communities. Search for carriers has therefore been abandoned as a method of control. Fortunately, in the general population, case to case infection is not common and it is unusual to get more than one case in a household. In dormitories or army barracks the living—and particularly the recreational—accommodation should be reviewed. Measures for the control of dust such as wet-sweeping or oiling of floors are useful. It is probably true to say that the danger of overcrowded sleeping-quarters and lecture halls is due more to the periodic disturbance of dust by movement than to the actual close proximity of the inhabitants. Good ventilation is also of great importance. It is possible that minor upper respiratory tract infections assist in the spread of meningococci, and in army camps, after a case has occurred, patients suffering from such complaints should be closely

examined. The occurrence of fever or headache should cause diagnostic procedures to be instituted forthwith.

Sulphonamide prophylaxis was extensively practised, especially in America, during the 1939-45 war, not always with happy results. Sulphadiazine in doses of 1.0 gm. daily was given and shortly after the onset of such treatment the carrier rate was greatly reduced; but when the drug was stopped, organisms reappeared in the throat with great rapidity—in some cases with a developed resistance to sulphonamides. This method of prevention, therefore, cannot be advised for widespread use. In army camps it has a place, but it is to be preferred that the drug be administered in full therapeutic dosage. Local treatment, for example with sulphonamide powders or penicillin lozenges, is not advised.

Where the disease is epidemic in a community it is well to remember that the highest attack rate is upon the child population under five years. The practitioner should endeavour to encourage hygienic living, especially for this age-group. Crowded assemblies, such as picture houses, should be avoided; and the sleeping together of adults and children in ill-ventilated rooms should, where possible, be forbidden.

### MENINGITIS

**Curative Treatment.**—*Sulphonamides.*—The use of the sulphonamide drugs has entirely replaced specific serotherapy. There are good grounds for believing that in man the combination of serum and sulphonamides achieves results inferior to those obtained with sulphonamide alone; the practitioner should not, therefore, use combined treatment.

The choice of drug is one which still elicits controversy. In the writer's experience the three common sulphonamides, sulphanilamide, sulphadiazine and sulphathiazole, achieve equally good results. In view of the nauseating effect of sulphapyridine, more especially in adults, the use of this drug should be discouraged.

Before instituting treatment, lumbar puncture must be performed. As much cerebrospinal fluid as possible should be allowed to drain away at this preliminary examination. Specimens should be submitted to appropriate tests. Since it may be some hours before the correct bacteriological diagnosis is obtained, treatment with sulphathiazole or sulphadiazine should be immediately instituted; if the infecting organism proves to be other than the *meningococcus*, these drugs will be equally effective. *The dosage to be described is suitable for a child of 2 years.* The doses of drug used are somewhat larger than those given in the table on page 75; in view of the serious nature of the infection at this age and the known low toxicity of sulphonamides in children there need be no hesitation in exceeding the usual dosage schedules during the initial stages of treatment.

0.5 gm. of the sodium salt (p. 77) should be injected intravenously. Intravenous administration is undoubtedly to be preferred; but this is one of the few occasions when deep intramuscular injection may be used if a suitable vein cannot be located.

0.75 gm. of the drug is administered by mouth. This dose should be continued four-hourly for the first 24-48 hours of treatment. If the clinical condition rapidly becomes satisfactory as judged by a fall of temperature and reduction of the other signs of meningitis such as headache and head retraction, the dose of drug may then be reduced to 0.5 gm. four-hourly.

Vomiting is a common feature in meningitis and often continues after sulphadiazine or sulphathiazole has been started. Should vomiting persist—and the organism is known to be meningococcus—there should be no hesitation in prescribing sulphanilamide.

*Fluids.*—It may be taken as invariably true that dehydration is present. Parenteral fluid is particularly necessary in infants and young children where fluid intake may be difficult to regulate; during the first twelve hours of treatment, from a half to one pint of warm sterile saline should be administered intraperitoneally, and this amount should be repeated twenty-four hours later in severe cases.

*Assessment of Progress.*—The best test of progress is the performance of a lumbar puncture 48 hours after treatment has begun. (To prevent loss of sulphonamide only a small quantity of fluid should be removed (5.0 c.c.) during the period of treatment.) In about 90 per cent. of cases no organisms can be found either on direct examination or after suitable culture. If organisms are still present, a further 0.5 gm. of drug should be given intravenously or intramuscularly and the higher oral dose continued for a further 24 hours. When organisms are present in the 48-hour specimen, lumbar puncture should be repeated at 24-hour intervals thereafter, until a sterile fluid is obtained. At every lumbar puncture Queckenstedt's test should be made to ensure patency of the cerebrospinal pathway. Should the C.S.F. pressure fail to rise with pressure over the jugular veins, blockage is present. In such cases cisternal or intra-ventricular injection of penicillin is worthy of trial (*v. infra*).

As a general rule it will be found that all physical signs have disappeared by the eighth or tenth days of treatment, and administration of the drug should then be stopped. Relapse occurs infrequently (about 2 per cent. of cases). It is a wise measure to regard any secondary rise of fever as a potential relapse; immediate lumbar puncture should be carried out and the fluid carefully examined for micro-organisms. The relapse should receive a course of treatment similar to that used during the primary attack; the course should be of longer duration and controlled by repeated lumbar puncture.

*Penicillin.*—Meningococcal meningitis should never be treated with penicillin alone. Given parenterally, the antibiotic passes the blood-brain barrier uncertainly and with difficulty. Should some special reason forbid the use of sulphonamides, large doses of penicillin must be ordered—500,000 units initially and 100,000 units every four hours—in the hope that some will penetrate to the meninges. Intrathecal penicillin will also be necessary, however. Penicillin of high purity should be used, and even then the maximum intrathecal dose at one injection should not exceed 15,000 units in a bulk of fluid less than that removed at lumbar puncture. The injection should be made slowly with a syringe, alternately injecting and withdrawing to ensure proper mixing with the cerebrospinal fluid. The injections should be repeated at least once every 24 hours, and twice during the first 24 hours.

The main indications for using penicillin are: (1) a very young patient; (2) extreme initial severity of the disease; (3) a suspected blockage at the base of the brain; (4) a poor response to sulphonamides.

- (1) In children under five years (and particularly under one) the prognosis is still severe. There is some evidence, albeit somewhat inconclusive, that the combination is better than sulphonamide alone.

- (2) If there is a profuse eruption, coma or severe vomiting, penicillin parenterally and intrathecally should be given. The lessened toxicity compared with sulphonamide may be of value in such cases during the preliminary period of treatment.
- (3) If blockage at the base of the brain is suspected, intrathecal penicillin at levels higher than the lumbar route should be used. Cisternal and even intraventricular injection is sometimes of help in refractory cases.
- (4) If organisms are still present in the 48-hour fluid or if relapse occurs, the administration of penicillin intrathecally may hasten cure.

It needs to be stressed that the exceptions—when penicillin should be used—are far outnumbered by the occasions when sulphonamide alone is successful. The tendency always to use penicillin in meningococcal meningitis is to be discouraged.

*General Management.*—Although the use of the sulphonamides has greatly shortened the acute stage of the disease (more than half of the cases are clinically and bacteriologically cured within four days), this should not diminish in any way the necessity for skilled nursing attention. This type of case, in fact, demands unremitting care from doctor and nurse alike.

Retention of urine still remains a common occurrence which should always be looked for, and, when present, catheterization should be performed. For the relief of headache, repeated doses of acetyl-salicylic acid will often be found effective. Chloral hydrate is a useful sedative. The writer always endeavours to avoid the use of morphine. Intense cephalalgia may often be relieved by lumbar puncture, but if a large amount of fluid is withdrawn it is probably wise either to increase the oral dose of sulphonamide temporarily or to give an intravenous injection of the drug.

*Complications.*—Broncho-pneumonia is the complication most to be feared. Although the pneumonia may be due to the *meningococcus*, in some cases cross-infection is the likeliest cause; masking of the attendants, the exclusion of adult visitors, and abundant fresh air for the patient are probably the best preventives and should be applied especially in young debilitated children. The use of sulphathiazole, in preference to sulphanilamide, may have a prophylactic action, by virtue of its wider antibacterial range.

Involvement of cranial or peripheral nerves may be expected in from 5-10 per cent. of cases. An unduly gloomy view of such complications is unjustified; a considerable proportion clear up satisfactorily. Blindness, often cortical in type, is usually permanent.

*Convalescence.*—The patient may be allowed out of bed towards the beginning of the third week of illness. A lumbar puncture should be performed on or about the 21st day of illness; the best criteria of recovery are a normal cell count and a normal content of sugar in the fluid, which should be clear. The patient may now resume normal activities and a reasonably long holiday should be advised. Adult patients often complain of a general weakness for some time after their recovery; as a rule the total duration of the illness will be from seven to ten weeks.

#### MENINGITIS DUE TO OTHER BACTERIA

Meningitis due to pneumococcus, streptococcus, staphylococcus and *H. influenzae* is almost always secondary to some other focus of infection

in the body. Should the bacteriological report incriminate one of these organisms, both sulphonamide and penicillin will be required. The treatment calls for the closest co-operation of physician, neuro-surgeon and bacteriologist and such cases should rarely be treated outside of hospital. The following are the main principles of treatment:—

*Sulphonamides.*—The dosage should be high and should be continued for a minimal period of ten days. Sulphadiazine is the drug of choice.

*Penicillin.*—Penicillin must be given systemically and intrathecally. To begin with, intrathecal injections may be required every 12 hours, but later once in 24 hours may suffice. The systemic penicillin will take care of the primary focus of infection which nowadays rarely requires urgent interference. Frequent bacteriological control of the C.S.F. is essential. Penicillin treatment can often be stopped after a period of five days, but the state of the patient and the condition of the spinal fluid will be the best indications of progress. For influenzal meningitis, a combination of streptomycin and sulphonamide has been advised, but at present it should be remembered that large doses of penicillin (1 mega unit per day) combined with sulphadiazine have given successful results.

*Relapse, Blockage and Brain Abscess.*—These complications are much more liable to arise from the organisms mentioned above than after meningococcal meningitis and must be kept constantly in mind. There must be no hesitation in performing lumbar, cisternal or ventricular puncture; any indication of rising intracranial pressure, especially in streptococcal cases, should raise the suspicion of abscess formation. The co-operation of the neuro-surgeon is essential for success. (See section on Nervous Diseases, p. 860.)

### CHRONIC MENINGOCOCCAL SEPTICÆMIA

This condition (the skin manifestation of which often closely resembles erythema nodosum) is particularly to be expected during epidemics. Unfortunately, blood culture, which is the essential method of diagnosis, is not always positive; at least twenty c.c. of blood should be withdrawn and the blood distributed in three or four bottles of broth. The bacteriologist should be advised regarding the type of case from which the cultures have been taken. A course of sulphathiazole or sulphanilamide appropriate to the age of the patient (most often an adult) should be given (see p. 74). The drug may be discontinued at the end of a week. Thereafter, the case should be observed for a few days, for the recurrence of fever, headache or skin rash. He may then be allowed up, and after a short convalescence may resume work.

### ACUTE MENINGOCOCCAL SEPTICÆMIA WITH ADRENAL HÆMORRHAGE

(See p. 441)

## CHICKENPOX

(*Varicella*)

A virus disease of high infectivity, chickenpox is probably spread by droplet infection and by conveyance of material from the skin lesions either on the hands or clothes of a third person, or possibly by air. The



incubation period is usually from thirteen to sixteen days. It is rarely less than eleven days or more than twenty days. There is good reason to believe that the disease is infective for at least twenty-four hours before the appearance of the rash. The duration of infectivity is uncertain, but for practical purposes may be regarded as persisting until the last primary crust has separated from the skin.

Chickenpox is not a notifiable disease, but should smallpox be prevalent in a particular area, chickenpox cases may have to be reported to the local Public Health Authority.

**Preventive Treatment.**—There is no effective specific method of prophylaxis against chickenpox.

Children who have not previously suffered from the disease should be kept away from school for twenty-one days from the date of last contact. Where the date of exposure is accurately known, quarantine need only be enforced from the tenth to the twenty first days inclusive.

Susceptible adult contacts need not stay away from their employment unless it involves close contact with children, *e.g.*, school teachers, nurses, etc.

Children who have not previously suffered from chickenpox should not be exposed needlessly to a case of herpes zoster.

**Curative Treatment.**—*General Management.*—The treatment of chickenpox is on general lines, no specific method being available. Even in mild attacks it is wise to confine the patient to bed during the efflorescence of the eruption. When the rash is profuse, bed should be enforced until the lesions have crusted. If there is a tendency to scratch the pocks, the hands may be wrapped in lint or gauze, or the arms lightly splinted.

The skin must be kept scrupulously clean by a daily warm bath, either coloured claret with potassium permanganate or to which a handful of boracic crystals has been added. After gentle drying, the skin should be dusted freely with either a good sterilized talcum powder or with a powder consisting of equal parts of boric acid, zinc oxide and starch. If itching is intense, the application of either calamine lotion or 2½ per cent. phenol in vaseline or olive oil will give relief.

In severe eruptions the whole skin surface should be painted daily with a 1 per cent. solution of permanganate of potash.

The light diet of the febrile stage can rapidly be followed by a return to normal food. A mild antiseptic mouth wash should be used after meals.

**Complications.**—Although complications are rare, secondary infection of the skin lesions with *S. pyogenes*, staphylococci or even the diphtheria bacillus may lead to serious and even fatal results. When infection has occurred the first step must be to ascertain the type of pathogen present. The administration of penicillin for the streptococcal or staphylococcal case will suffice. If *C. diphtheriæ* is the cause, serum of course must be given.

**Convalescence.**—Chickenpox is one of the mildest of the infective diseases, and no special measures are required during convalescence. Isolation should be continued until the last primary crust has separated from the skin. Work or school may be resumed a day or two after release from isolation.

## DIPHTHERIA

Diphtheria is almost entirely a toxic disease. Although some slight tissue invasion takes place in severe infections, for the most part the organ-

isms remain localized to the site of inoculation from which the toxin diffuses by lymphatics and blood stream to all parts of the body. The ability of the host to neutralize toxin thus constitutes an almost complete defence; for shorn of its toxic action the diphtheria bacillus is a weak pathogen.

*C. diphtheriae* is now divisible by cultural methods into three main types—*gravis*, *intermedius* and *mitis*. Broadly speaking, the first two are associated with a more severe form of the disease, although typing is not of immediate importance to the clinician who must assess the initial treatment before such information is available. The subsequent progress of the case, however, should be governed to some extent by the results of typing; *gravis* and *intermedius* infections should generally be allowed more careful and prolonged convalescence. Further, almost all *gravis* and *intermedius* strains are virulent, so that a carrier of these types may be regarded as harbouring pathogenic organisms. *Mitis* strains are frequently non-virulent and a virulence test is essential before the final assessment of a carrier can be made. The importance of typing in epidemiological work will be obvious.

Cases and carriers constitute the main sources of infection. Usually the bacteria are carried in the throat or nose, the latter site being rather more common, so that in a search for a source of infection nasal cultures should never be omitted. Cutaneous diphtheria, often masked as a chronic sore, may be an unsuspected source of infection. Although in most instances infection is spread by droplet infection, contaminated milk, ice-cream and food have initiated local outbreaks.

Diphtheria is a notifiable disease and has an incubation period of two to five days.

The importance of the early diagnosis of diphtheria cannot be too strongly emphasized. Careful examination of the fauces should be a routine procedure in every febrile case. Apart from the presence of "false membrane," marked faucial and palatal oedema, accompanied by an acute gross enlargement of the cervical glands, should, in a child, always be treated as diphtheria until proved otherwise.

**Prevention and Epidemiological Control.**—*Schick Test.*—Susceptibility to diphtheria can be ascertained by the application of the Schick test—an intradermal injection into the left forearm of 0.2 c.c. of diluted diphtheria toxin. Individuals showing an area of erythema from 1 to 4 cm. in diameter around the site of injection four to seven days after the application of the test are said to be Schick positive, an indication of susceptibility to the disease. When applying the primary Schick test to a large community the highest proportion of positive results will be obtained when the reactions are read on the seventh day. No local reaction appears in those who are immune (Schick negative reactors). In individuals above nine years of age a precisely similar injection is made into the skin of the right forearm, but with toxin which has been previously inactivated by heat. This control test enables us to discriminate between local reactions arising from sensitization to the protein present in the test fluid and the true positive Schick reaction. Reliable Schick and control test material can be obtained commercially.

Among children in this country the proportion susceptible to diphtheria varies from 15 to 90 per cent. according to age and social environment; the highest proportion of susceptibles is found in the pre-school age group and among the well-to-do.

*Active Immunization.*—Every child should be actively immunized against diphtheria as soon after its first birthday as possible. A preliminary Schick test may be omitted.

Various immunizing preparations, termed diphtheria prophylactics, are available commercially, of which the best are alum precipitated toxoid (A.P.T.), formol toxoid (F.T.) and toxoid-antitoxin floccules (T.A.F.). Two intramuscular injections of 0.2 and 0.5 c.c., respectively, of alum toxoid, administered at an interval of four weeks, will render at least 95 per cent. of children immune to diphtheria within six weeks of the final injection. In those very rare cases in which the reaction to the first dose of 0.2 c.c. A.P.T. is severe, the second injection should be modified to 0.3 c.c.

The first injection merely acts as a "priming" stimulus and has no permanent effect in inducing immunity. It is the second stimulus which provokes a high level of antitoxin in the blood, a level which falls rather slowly during the next twelve months. No reliance whatsoever should be placed on the immune status of an individual who has had a single injection of any of the diphtheria prophylactics. *Formol toxoid* is liable to be followed by unpleasant side-effects when injected into persons over 8 years of age, and although used effectively abroad, has never been popular in Great Britain. *Toxoid-Antitoxin Floccules* has the advantage of being particularly free from unpleasant reactions and is the safest prophylactic for children over the age of 8 years. It has the slight disadvantage that it contains horse serum. The course consists of three injections each of 1.0 c.c. at intervals of two to four weeks. For all of the prophylactics the injections should be made intramuscularly either into the deltoid or into the fleshy muscles below the spine of the scapula.

From four to eight weeks after completion of the immunizing course, evidence of satisfactory immunity should be obtained either by the application of the Schick test or by the estimation of the antitoxic content of the blood. The latter procedure is the more reliable but is not practicable in general practice. Should susceptibility still persist, as indicated by a positive Schick reading, the immunizing course must be repeated and a re-test applied one month later. Adults are more resistant to immunizing procedures, and if the risk of exposure is great it is advisable to carry out Schick tests.

Although absolute protection against diphtheria cannot be guaranteed in every individual who has completed the immunizing course, marked modification in the severity of a subsequent attack is to be expected. The duration of immunity varies, but in all except a small percentage of children lasts for some years. The important consideration is that the child has been trained in antitoxin production so that a small dose of antigen subsequently will evoke a sharp rise in antitoxin. The next period of danger in the child's life is when entering school, so that a single intramuscular injection of 0.2 c.c. alum toxoid when the child commences his school career should be regarded as an essential part of the prophylactic course. The immunizing injections do not, with rare exceptions, give rise to marked local or systemic disturbance in young children.

*General Measures.*—For the control of an outbreak the first steps are the isolation of the case and the disinfection of all articles likely to be contaminated with the faucial or nasal secretions of the sick person. Household or institutional contacts must be carefully examined for evidence of a

missed infection. Individuals with chronic nasal or aural discharge, obviously unhealthy tonsils—or a suspicious cutaneous lesion—should be isolated, and swabs taken from nose, throat or other suspicious site.

Indiscriminate swab-taking from all contacts as a measure of control should in general be avoided, for “positive” reports on microscopic examination at 24 hours may be misleading and typing will usually take three or four days to complete. When the outbreak is confined to the occurrence of a single case, careful clinical supervision of the remainder after the removal of those with unhealthy conditions of the nose, throat or ear will usually suffice. The latter group should be carefully tested for the presence of a carrier. *All contacts should be examined daily for seven days* and, on the slightest suspicion of clinical infection, antitoxin in therapeutic doses should be administered. Knowledge of the type of organism in the primary case is of importance, for it will focus attention on the type to be looked for in the carrier. Not infrequently more than one type will be discovered in the examination of carriers and it must be again pointed out that virulence tests on mitis organisms are essential. All carriers of *gravis* and *intermedius* strains may be regarded as dangerous.

The use of antitoxin as a sole means of prevention is not advised. When it is used, 500 to 1,000 units should be injected into one arm and this should be accompanied by an injection of 0.3 c.c. of alum-precipitated toxoid into the opposite arm, the course being completed by a second injection of the latter, one month later. This method of combined passive and active immunization has much to commend it.

The Schick test is of value in dividing the contacts into susceptibles and immunes and should immediately be used when more than one case of diphtheria occurs. Schick negative individuals should be examined carefully by nasal and pharyngeal swabs, attention being paid not to the initial “microscopic” report but to the more definitive report after typing has been completed. After two negative swabs, these individuals may be released from surveillance. All carriers of virulent organisms must be isolated and treated. Schick positive individuals should be given combined passive and active immunization and kept under clinical supervision for seven days.

It must be remembered that a history of immunization should not lead the practitioner to ignore the possibility of diphtheria. Indeed it must be emphasized that the appearance of the throat in such cases is often so atypical that the lesion is more suggestive of tonsillitis. Further, although it is undoubtedly true that the disease in the immunized is often mild, failure to make an early diagnosis may result in the administration of serum too late to prevent nervous complications. It might not be too paradoxical to suggest that at the present time, with the numbers of immunized still inadequate, it is even more necessary than ever for the practitioner to acquire the habit of injecting from 4,000 to 8,000 units of serum when, in a suspicious case, a history of contact or the appearance of the throat suggests the necessity of a swab examination. It is not sufficiently realized that 4,000 units of the new refined diphtheria antitoxin is contained in a bulk of only 1.0 c.c., and that the liability of serum reactions occurring with this product is so small as to be negligible. Finally, it should be noted that the modern fever hospital is usually prepared to receive cases for “observation.”

**Curative Treatment.**—The four essentials in the treatment of a case of diphtheria are: (1) early adequate serum administration; (2) absolute rest

in bed for a varying period of time according to the severity of the disease; (3) skilled nursing; and (4) the free administration of glucose.

**Antitoxic Serum.**—An intramuscular injection of at least 4,000 units of diphtheria antitoxic serum should immediately be administered to any patient suspected to be suffering from diphtheria. *Bacteriological confirmation of the clinical diagnosis should follow and not precede the administration of antitoxin. When the clinical picture is typical of diphtheria, negative bacteriological findings should be ignored and adequate serum treatment immediately instituted.* There is considerable difference of opinion regarding the optimum dosage of antitoxin in the treatment of diphtheria. Broadly speaking, mild attacks should receive from 4,000 to 8,000 units intramuscularly; cases of moderate severity from 10,000 to 30,000 units intramuscularly; severe or toxic attacks from 50,000 to 100,000 units of antitoxin intravenously. When the diphtheritic infection is limited to the larynx, 10,000 units of antitoxin is usually sufficient, and in purely nasal diphtheria, unless toxæmia is severe, 4,000 to 8,000 units is adequate.

In endeavouring to assess the *amount* of serum required, three clinical estimates may be combined—

- (i) Although no amount will compensate for delayed administration, a case seen late should receive a large dose of antitoxin.
- (ii) In general, the more membrane, the more toxin formation and therefore the greater need for a large dose of antitoxin. In particular, large doses should always be given when the membrane extends to the uvula, nasopharynx or soft palate. (It should be remembered that severe gravis infections often show a small amount of true membrane but tremendous œdema and “glairiness” of the soft palate, simulating quinsy. Such cases should always receive a large dose.)
- (iii) Extensive enlargement of the tonsillar glands calls for a large dose of serum.

There is no satisfactory method of assessing the correct amount of antitoxin, so that it is better to err on the side of overdosage. There are good grounds for believing that a dose of 50,000 units is more than adequate for the most severe case of diphtheria and that it should never be necessary to give more than 100,000 units.

The *route of administration* is of as great importance as the amount of antitoxin. It is rarely appreciated that a considerable time elapses after intramuscular injection before “peak” levels are attained in the blood stream. *All severe cases (i.e., where more than 36,000 units are to be given) must receive at least part of the dose intravenously.* When, by reason of collapse of veins, this is not possible, the serum should be given intraperitoneally. In other words, the intramuscular route is the third-best route and should only be used in mild or moderate cases. Intramuscular serum should be given into the middle third of the outer aspect of the right thigh. For the patient who must lie on his back this permits him to turn on his left side and use his right arm with comfort.

**Other Specific Treatment.**—The bacteriological examination of the throat swab should include search for Vincent's organisms by direct film, and for other pathogens—particularly *S. pyogenes*—by suitable culture. The sulphonamides and penicillin have no direct application to the initial treatment of the diphtheria. Although there have been a few favourable reports

in regard to penicillin, they are not convincing; but when there is super-added infection, penicillin is worthy of a place. It should be given systematically in large doses (50,000 units four-hourly) in order to ensure an adequate concentration at the local site. Penicillin lozenges are not advised. The lack of toxicity of penicillin makes its use more desirable than sulphonamides.

*Glucose.*—Glucose lemonade should be freely administered to every diphtheritic patient. Glucose, indeed, constitutes the best cardio-vascular tonic and administration of a 5 per cent. glucose-saline infusion is often advised with the initial intravenous serum. Large intravenous infusions are, however, to be avoided in severe infections, and it is therefore preferable to give 100-200 c.c. of a 25 per cent. glucose solution, repeated, if necessary, at eight-hourly intervals.

*General Measures.*—With the exception of the mildest attack a case of diphtheria should not be treated at home unless fever-trained night and day nurses can be provided. From the moment that diphtheria is suspected, the patient must be confined to bed in a strictly recumbent position. Owing to the risk of cardio-vascular complications, any attempt to sit up, reach over to a chair or bedside table, etc., must be strictly prohibited. The patient should not even feed himself. The period of recumbency varies from fourteen days in mild attacks to eight weeks or longer in severe cases, according to the condition of the cardio-vascular system and the incidence of paralysis. The need for strict recumbency is not dictated solely because of cardiac damage, but because the peripheral circulation is also severely affected.

After the addition of a second and a third pillow at intervals of two clear days, the patient is permitted to sit up, and may leave his bed seven to ten days later. The rate of progress will vary according to the severity of the attack and the response of the cardio-vascular system to increased exertion. Care should be taken to curtail activity when the patient gets on to his feet.

A fluid diet with the addition of ice-cream and jellies is the most suitable so long as the throat is inflamed. A glucose intake by mouth of from 3 to 5 oz. daily in the form of glucose lemonade is of definite therapeutic value. As the throat improves the diet may be increased and varied, but food must still be given in small amounts at two-hourly intervals and indigestible articles carefully excluded.

When grossly inflamed and foul or necrotic, the throat may be douched two-hourly with either warm normal saline or bicarbonate solution, and small pieces of ice sucked. No good purpose is served by persisting in local treatment if the child resents it. The consequent struggling does more harm than the douche does good. In most cases of diphtheria local treatment is unnecessary. The mouth should be cleansed after each feed. Hot fomentations may be applied to the neck if the swollen cervical glands are painful.

Except in slight attacks, when mild aperients may be administered, the bowels should be opened by enemata every alternate day.

The possible development of ocular paresis requires to be borne in mind and reading restricted to two hours daily; the print must be large and the page well illuminated.

*Complications.*—The prevention of serious toxic damage to the heart and vessels by the early application of the measures detailed above is the funda-

mental principle in the treatment of diphtheria. Once well-marked signs of cardio-vascular weakness appear, little can be done to ward off death. The foot of the bed should be raised. Vomiting due to cardiac failure necessitates the replacement of oral feeding by the regular administration of rectal or intravenous glucose salines. The mouth may be moistened with sips of water or pieces of cracked ice. Epigastric pain, restlessness and anxiety are best relieved by repeated hypodermic injections of morphine:  $\frac{1}{8}$  gr. (2 mg.) for a child of two years,  $\frac{1}{4}$  gr. (4 mg.) at five years, and  $\frac{1}{2}$  gr. (5 mg.) for a child of ten years.

The various vasomotor or cardiac stimulants have no place in the treatment of circulatory failure in diphtheria. In view of the damage done to the suprarenals in severe diphtheria it is worth considering the use of desoxycorticosterone acetate. A daily dose of 5-15 mg. should be given when the systolic pressure falls below 100 mm. This oily solution, because of its slower absorption, is to be preferred to the watery extracts whose effect is transitory.

Digitalis or strophanthus are definitely contraindicated. The routine administration of alcohol has nothing to commend it.

Apart from involvement of the pharyngeal and respiratory muscles no anxiety need be felt regarding the outcome of the post-diphtheritic palsies, since they tend to recover spontaneously within a few weeks. In palatal paresis the fluid part of the diet should be replaced by semisolids. In pharyngeal paralysis the foot of the bed should be raised 18 in., saliva and mucus aspirated at frequent intervals from the pharynx and food administered by the nasal tube. On the slightest indication of weakness of the intercostal or diaphragmatic muscles the patient must be treated in a mechanical respirator.

Late generalized muscular weakness improves with massage, hot and cold douching, graduated exercise, fresh air and good food.

**Convalescence.**—It is advisable to obtain two consecutive negative cultures at an interval of one week from both throat and nose before the patient is released from isolation. Even after a mild attack the patient should not resume school or work for at least a fortnight after release from isolation. The convalescent period may require to be prolonged to six months or even longer following toxic diphtheria. Strenuous exercise must be forbidden during convalescence. A change of air to the country or seaside and the administration of iron is very beneficial.

## CARRIERS

The first essential in dealing with a persistent convalescent or contact carrier of morphological diphtheria bacilli is to ascertain whether the organisms present are virulent or non-virulent. Carriers of non-virulent bacilli are not dangerous to the community and need not be segregated.

The next essential is to make a careful examination of the nose or throat for the presence of abnormalities. As a general rule, the carrier state is associated with unhealthy tonsils or adenoids and even carious teeth may act as a focus and prolong the condition. In open diphtheria wards the final possibility exists that the individual may acquire the organism by cross-infection. The convalescent patient, mixing freely with others and often coming in close contact with recently admitted cases, may be the

subject of continual reinfection. A period of complete isolation often proves effective in clearing the carrier state, and since it is always necessary to be cautious before subjecting the convalescent diphtheria patient too hastily to operative procedures, a period of cell-isolation along with local treatment should always be given a preliminary trial.

Sulphonamide or penicillin, either alone or in combination, are probably the best antibacterial agents, although it is well to remember that they are not always successful. The three best methods are—

*Insufflation of powder locally to the nose and throat.*—The powder consists of sulphathiazole into which has been mixed penicillin in a strength of 5,000 units per gm. The powder should be used four-hourly during the day.

*Penicillin spray.*—An atomized spray of penicillin in saline (5,000 units per c.c.) may be used hourly by inhalation into the nose and throat.

*Systemic penicillin.*—A five-day course of 300,000 units of penicillin daily is worthy of trial.

Should isolation and one or other of these methods fail, surgical interference is indicated. Before release from isolation, three consecutive negative cultures from nose and throat, taken at 48-hourly intervals, should be obtained.

### LARYNGEAL DIPHTHERIA

On the slightest suspicion that a child is suffering from a diphtheritic laryngitis, the practitioner should immediately inject 8,000 units of antitoxin intramuscularly and arrange for the prompt removal of the patient to hospital. The steam kettle, hot fomentations to the neck and the administration of 10 to 20 minims (0.58 to 1.2 c.c.) of camphorated tincture of opium every four hours are helpful in the early stages of the attack. Recent experience suggests that penicillin (50,000 units four-hourly) is always worthy of trial.

In hospital practice the diagnosis can be confirmed by endoscopy, and relief of respiratory distress attained either by aspiration, intubation or tracheotomy.

Laryngeal diphtheria calls for constant watchfulness, skilled care and highly specialized treatment. In an emergency the practitioner may be called upon to perform a tracheotomy. The reader is referred to surgical textbooks for the appropriate technique.

### BACILLARY DYSENTERY

Dysentery must now be regarded as an endemic infection in large cities. Notifications of the disease have increased greatly in recent years, and in view of the mild nature of the symptoms in many cases it may be assumed that the notifications represent but a proportion of the actual incidence. There is a slight trend towards a seasonal incidence which is maximal between July and November. A large proportion of the infections are in children under 15 years of age, in whom the disease often runs a very mild course. It is not sufficiently well known that the presence of blood or mucus is not a necessary accompaniment of the diarrhoea and that loose green coloured stools are common. As a result, many infections are missed and so increase the spread of the disease. Some convalescents become temporary carriers and act as a source of infection.



Dysentery is thus spread in the same way as enteric fever, namely, by the transference of faecal material from missed cases or carriers to the food of others. The infection is particularly liable to arise in epidemic form in closed communities: day nurseries and children's homes require particular care in this respect. As a commentary on the changed nature of the disease it has been well said that "what was once the scourge of armies has now become the bane of day nurseries."

A number of organisms is responsible for the disease, but in Great Britain Flexner and Sonne types of *B. dysenteriae* account for the great bulk of infections. Shiga strains, which give rise to a serious form of the disease in the tropics, are rarely encountered in this country.

Unlike enteric fever, the infection remains almost entirely localized to the bowel and agglutinins do not appear in the blood to any great degree. Apart from the toxic absorption due to bowel ulceration, the main damage arises from the exhaustion of the patient by loss of fluid and salt in watery stools. This results in dehydration and hypochloræmia, the degree of which is dependent upon the character of the stools and the duration of diarrhoea.

Diagnosis depends on accurate bacteriological examination. For the purpose a rectal swab outfit is to be preferred since the specimen can be secured quickly and easily. No time should be lost between obtaining the specimen and submitting it to the laboratory. The use of the rectal swab combined with improvement in selective media has added great precision to the diagnosis.

Dysentery is a notifiable disease.

**Prevention and Epidemiological Control.**—The control of ward and institutional outbreaks often presents an overwhelming task. All further admissions should be stopped and a close search made for carriers and missed cases, both among patients and staff. The bacteriologist should be brought into consultation at once, for the addition to his routine work will be considerable and he should therefore be forewarned. Plans should also be prepared for the separation of those individuals found to give positive results and arrangements made for the sterilization of food utensils, bed-pans, etc. Soiled napkins should be dropped direct into pails containing dettol. The nursing staff must be instructed regarding the method of transference of the infection and basins of dettol placed suitably so that hand disinfection after any bed manipulations can be easily carried out. The nurses should also be taught that the simplest case of diarrhoea may well be dysentery and that the occurrence of a loose or green stool should be reported at once.

The administration of sulphasuxidine to all contacts in therapeutic doses is justifiable and undoubtedly limits spread. Indeed, in children's homes and residential nurseries a routine course of sulphasuxidine in full dosage for five days to all new admissions before they are allowed to mix with the older patients has proved successful in lowering the incidence subsequently in the institution.

Before known positive cases or carriers are permitted a return to freedom, a series of six negative rectal swabs should be demanded. The convalescent carrier of dysentery has not received the emphasis he deserves, and laxity in bacteriological control prior to dismissal is a common cause of fresh outbreaks.

**Curative Treatment.**—The majority of cases, due to Sonne and Flexner

infections, run a mild course of three or four days and call for little medicinal treatment. The administration of specific serum to cases of Shiga infection is of undoubted value. The dose is up to 100 c.c. and the injection should be given intravenously.

**Sulphonamides.**—Because of their relatively poor absorption, sulphaguanidine and sulphasuxidine can be given in much larger doses than the other sulphonamides with a virtual freedom from toxic effects. This is an advantage in the treatment of a disease where dehydration is marked. Apart from this freedom from toxicity, however, these drugs show no advantage over sulphadiazine; for dosage and technique of administration see p. 76.

Although the mildness of the symptoms may often suggest little need for specific treatment, the stools are rendered non-infectious more rapidly and the risk of the development of the carrier state reduced by the early administration of sulphonamides.

**General Management.**—The patient must be confined to bed and kept warm from the first symptom of the disease. Except in the mildest attacks the bed-pan should be employed in order to avoid contamination of lavatory seats, etc. When the call to stool is incessant the bed-pan may be dispensed with and the motions received into tow which, when soiled, is collected and burnt. Specimens of stool must be collected daily for inspection by the practitioner.

Provided the diet prescribed is nutritive, easily assimilable and with little residue, considerable latitude is permissible. During the acute stage albumen water, arrowroot, jellies, thin gruels, chicken-tea and clear soups may be given in small amounts at two-hourly intervals. Casein hydrolysates are worthy of trial although their value is not always apparent. Carbohydrates should be given in a dextrinized form as crisp toast. As the symptoms abate, milk, cream, butter, puréed fruit and eventually carefully sieved and puréed vegetables may be added very gradually to the diet.

When diarrhoea is excessive, a rectal irrigation of warm saline, followed by the administration of either an enema containing 40 minims (2.32 c.c.) of tincture of opium in one to two ounces of starch mucilage, or a suppository containing  $\frac{1}{4}$  gr. (16 mg.) morphine, should be prescribed for the relief of tenesmus. If irrigations afford relief and are well borne, they may be repeated twice daily during the febrile period. Pain, due to griping or colic, may be severe. Hot application to the abdomen may be helpful, but when severe, tincture of opium in doses of 5 minims (0.3 c.c.) four-hourly will usually alleviate the symptom. Occasional cases develop *chronic dysentery* which can be very resistant to treatment. Retention enemata may alleviate these and the use of 12 gm. of sulphasuxidine in the enema is worthy of trial. Silver nitrate enemata have also proved efficacious, the enema consisting of 6-8 ounces of water containing  $\frac{1}{2}$  gr. (0.03 gm.) of silver nitrate to the ounce to be retained as long as possible. Since the routine use of the sulphonamides, however, such cases have become exceptional. It is usually prudent to advise care in the diet for some time after the attack, especially in adults. Foods with a bulky and rough residue should be particularly avoided.

**Carriers.**—A course of sulphasuxidine should be administered to all persistent carriers of dysentery bacilli (see p. 76). At least six consecutive negative stool cultures over a period of four weeks must be obtained before reasonable certainty of cure is assured.

## ENTERIC FEVER

(*Typhoid and Paratyphoid Fevers*)

The annual occurrence in Great Britain of one or more epidemics of enteric fever indicates that, in spite of sanitary precautions, the risk of contamination of water and food supplies with the enteric group of organisms still persists. *B. typhosus* and *B. paratyphosus* B, the organisms commonly met with in the British Isles, are excreted in the stools and urine during the course of the illness. The unsuspected ambulant case, the missed case, the temporary carrier and the chronic carrier play a very important part in the dissemination of enteric fever. It is estimated that from 2 to 5 per cent. of all cases of enteric fever become permanent carriers. That the incidence of the chronic carrier state is four times higher in women than in men is unfortunate when we consider the possibilities of contamination of food in course of preparation. Although the faecal carrier is more commonly encountered, the urinary carrier is potentially more dangerous. The organisms are discharged intermittently in both stools and urine, so that repeated bacteriological examinations are essential before the carrier state can be excluded.

Although isolation of the pathogen from faecal and urinary specimens is the only exact method of diagnosing carriers, preliminary examination of the blood serum may serve as a useful "screening" test when large numbers of suspects have to be reviewed. Antibodies for the Vi antigen are almost always to be found in fairly high titre in carriers; so that if a preliminary blood test is carried out attention can be directed particularly to those with such antibodies.

Outbreaks, then, are usually a result of the contamination of food or water by a case or carrier. Milk or milk products, prepared meats, uncooked vegetables, fruit and shellfish constitute the usual vehicles of infection. A nurse may contract the disease in the course of her duties; this usually indicates carelessness in the washing of hands. It is important to make a specific prohibition of the eating of any food by the attendant in the ward or room where the disease is being nursed.

• The incubation period of enteric fever varies from four to twenty-four days; in typhoid infection the most usual period is twelve to fourteen days, and in paratyphoid B from ten to twelve days.

\* Enteric fever is a notifiable disease.

**Prevention and Epidemiological Control.**—The control of enteric fever is essentially a problem for the local Sanitary Authority and embraces such factors as an efficient system of sewage disposal, a safe water and milk supply, the detection of carriers, the purification of shellfish, the control of the house-fly and protection of food against contamination by rats and mice.

Careful supervision of sewage and water is a commonplace in the large towns, so that widespread epidemics of typhoid are now unusual. In country districts, however, defective cesspools, flooding or ineffective disposal of sewage are still commonly the source of localized outbreaks. Milk, and particularly ice-cream, is now replacing water as the vehicle of infection, particularly of paratyphoid fever, and here the towns are in as much danger as the countryside; but although day-to-day control by Public Health

Departments forms an important part of the protection of the public, the early diagnosis of the infected case by the practitioner is of prime importance both in stemming an incipient epidemic and in stopping it once it has started. The value of early blood culture in cases of continued fever must here be appreciated; and the golden rule should be *to carry out a blood culture on any case which has an unexplained pyrexia for more than three days*. A specimen of blood for agglutination tests should be submitted at the same time. The impression that it is only worth while to examine for agglutinins after the end of the first week of illness is quite erroneous. An early specimen may show their presence in low titre, and if a further examination in three or four days shows a rise in titre the diagnosis is almost certain. Previous inoculation, of course, against typhoid or paratyphoid, to a large extent invalidates the Widal test and no reliance can be placed on the results in such persons.

Of great assistance in tracing the exact source of the epidemic has been the subdivision of the typhoid group by specific bacteriophages into a number of "phage" types. This has placed in the hands of the epidemiologist greater precision in attributing cases to a particular carrier.

Where a number of cases occurs in a district, the practitioner will usually be informed by the local Public Health Department, and co-operation with it in attempts to investigate the source of the epidemic will be of the greatest benefit. The practitioner is in a favourable situation for seeing "formes frustes" examples of infection and he should bear in mind the fact that many of the illnesses, especially of paratyphoid fever, are mild; they may be unaccompanied by any diarrhoea and may easily masquerade as influenza, tonsillitis or bronchitis. In his daily practice, too, he should insist on the boiling of water and milk and in the avoidance of all foods eaten in a raw or partially cooked state. A campaign against flies should be instituted, and here the use of D.D.T. plays an important part.

*Vaccination.*—T.A.B. vaccine usually contains 1,000 millions of *B. typhosum* and 500 millions each of *B. paratyphosum A* and *B* in each cubic centimetre. The initial dose in adults is 0.5 c.c. followed seven to ten days later by 1.0 c.c.; to children between three and ten years of age 0.25 and 0.5 c.c. may be administered. A third injection of 1.0 c.c. (adult) or 0.5 c.c. (child) should be administered one week later if the individual is going to reside in an endemic area. The injection is given subcutaneously below the scapula, and as systemic disturbance is liable to follow, the individual should avoid any strenuous exertion for twenty-four hours after each dose. Contraindications to inoculation are pulmonary tuberculosis, diabetes mellitus and chronic kidney or vascular disease. The vaccine should not be administered during late pregnancy or during the course of an acute infection.

Protection is attained within two weeks of the final injection, and after lasting for some months gradually lessens over a variable period. Re-immunization every twelve to eighteen months by a single dose of 0.5 c.c. intramuscularly is a wise measure should the danger of contracting the disease persist.

Recent work has emphasized the importance of the stimulation of antibodies to the Vi antigen in order to gain good protection. Vaccines where the organisms are killed by heat and preserved with phenol tend to be poorer in Vi antigen and other preservatives are therefore under investigation. At present, the vaccine where the organisms are killed by alcohol and preserved by alcohol is advised. For males, a first injection of 0.25 c.c.

is followed 3-4 weeks later by a dose of 0.5 c.c. For females the corresponding doses are 0.2 c.c. and 0.4 c.c. It is advised that these doses should not be exceeded.

This continued search for an improved vaccine draws attention to the fact, not always appreciated, that individuals satisfactorily inoculated sometimes contract enteric fever. A potent antibacterial immunity is clearly not always acquired. A previous history of inoculation, therefore, must not be taken to exclude the possibility of a diagnosis of enteric fever. The individual risk of contracting the disease is, however, greatly diminished, and no one should enter an area where enteric fever is endemic nor should a person nurse the disease unless previously immunized. In the face of an actual epidemic, especially if the number of cases is increasing and the source still undiscovered, the question often arises as to whether contacts should be inoculated. It is now generally agreed that "provocation typhoid" is a negligible risk and that in such circumstances immunization should be undertaken.

*Passive Immunization.*—The prophylactic value of antityphoid serum has not yet been proven and requires further investigation. The prophylactic dose of antityphoid serum advised for an adult is from 20 to 30 c.c. administered intramuscularly. Passive immunization should be confined to home or institutional contacts who have been exposed recently and intimately to typhoid infection.

*Curative Treatment.*—*Chemotherapy.*—The sulphonamides alone have proved of no value in the treatment of the enteric fevers. Indeed, the known toxic effect of the sulphonamides upon the bone marrow, which is already severely depressed in typhoid, would suggest that they should be used with great caution. There are grounds for believing, however, that a combination of sulphonamides and penicillin may have a synergistic action on the typhoid group of organisms, and accordingly the administration of such combined therapy has been used with success. The daily dosage is 2.5 mega units of penicillin divided into ten injections at two-hourly intervals; and 8.0 gm. of sulphathiazole given in one-gram doses every three hours. Such intensive treatment should be concentrated into a four-day course. If beneficial results have not been obtained, the course may be repeated, and during the second course the dose of penicillin should be increased to 3.0 or 4.0 mega units per day. A careful watch should be kept on the white cells, a count of which should be performed prior to the commencement of and repeated daily during the course.

*Serum.*—The reports so far published on the therapeutic value of the antityphoid serum have been favourable. Marked and rapid improvement sometimes follows serum administration in some cases of typhoid fever, but not in all.

Serum should be administered to severe cases as early as possible in the course of the disease in an initial intravenous dose of 60 c.c., followed by a daily intramuscular injection of 30 c.c. on each of the three or four succeeding days. The danger of serum reactions must be emphasized and the initial dose should be given gradually after preliminary injections of small doses. Adrenaline should be at hand.

*Vaccines, etc.*—Typhoid vaccine and various forms of non-specific therapy are not entirely devoid of risk and cannot be recommended.

*Bacteriophage.*—The published reports on the value of D'Herelle's bac-

terioophage in the treatment of typhoid fever are so conflicting that it may be reasonable to assume that the preparation is of doubtful value.

*General Management.*—A practitioner who undertakes the treatment of a case of enteric fever must not only satisfy himself that the home arrangements and resources are adequate and that two nurses experienced in the management of the disease are available, but must also be prepared to visit his patient at least twice daily for a period of some three to four weeks. Hospital is the ideal place for treatment, and it is very important that the patient should be removed there at an early stage of the illness.

The patient must be kept strictly recumbent, but his position should be altered several times daily. Mental rest is essential, and visitors should be excluded. A four-hourly chart must be kept and arrangements made for the prompt notification of serious symptoms to the physician. Stools, urine and other discharges, wash water, soiled linen, nursing utensils, etc., require to be carefully disinfected, and the patient's crockery, cutlery, etc., must be boiled after use. Measures should be taken to rid the sickroom of flies. The nurse must on no account prepare or handle food which is to be consumed by other members of the household.

The mouth and skin require regular and careful cleansing, and precautions have to be taken to prevent the development of pressure sores.

Retention of urine is liable to occur and should receive appropriate treatment. Inspection of the stools, abdomen, lung bases and heart should form part of the physician's daily routine examination.

*Diet.*—Although Ker successfully treated many hundreds of cases of enteric fever with a diet limited to milk and beef tea, modern opinion rightly favours a more liberal diet. It is very difficult to get a typhoid patient to take nourishment, but with the aid of a tactful nurse and careful attention to the patient's idiosyncrasies a daily intake of at least 2,000 calories may be attained. During the early days of the illness a fluid diet should be administered. Towards the end of the first week, in addition to 2 pints of milk daily, such readily digestible articles as lightly boiled eggs, custard, ice-cream, junket, cream cheese, milk shapes, milk puddings, jellies, mashed potatoes with butter or gravy, prepared breakfast foods, stewed apples, plain chocolate, thin bread and butter, sponge cake, and minced chicken or beef may be administered. Not more than 5 oz. of milk should be administered at one time and each feed should be consumed within fifteen minutes.

Feeds should be given at two-hourly intervals, between 7 A.M. and 9 P.M., and twice during the night when the patient is awake.

Plain cold water or fresh orange, lemon or grapefruit drinks sweetened with lactose or glucose should be administered at least every half-hour between feeds. A daily fluid intake, apart from meals, of at least 4 pints is desirable. An occasional cup of weak tea may be appreciated.

*Complications.*—*Constipation.*—Constipation is almost always present in the early stages. Purgatives should never be used. The best method of management is to order a simple wash-out—allowing the contents of the bowel to syphon back—every two days. Liquid paraffin, in a dose of 2 drachms (7.2 c.c.) every four hours, may safely be prescribed in convalescence to encourage normal bowel movements.

*Diarrhœa.*—Severe and persistent diarrhœa necessitates restriction and modification of the diet. If curds are present in the stools, milk should be

restricted in amount, diluted or peptonized; it may be necessary to replace milk by whey. The carbohydrate intake should be diminished, lactose substituted for glucose and soups excluded. Colonic lavage with warm water or saline once or twice daily followed by a starch and opium enema in the evening is a useful procedure. An occasional dose of 5 gr. (0.3 gm.) of Dover's powder is often effective in lessening the frequency of the motions.

*Meteorism.*—On the first indication of increasing abdominal distension the diet must be restricted as for the treatment of diarrhoea. If meteorism becomes severe, food should be restricted to whey, albumen water and cold meat juice. A soft rubber catheter should be introduced some 12 in. into the rectum and left *in situ* for twenty minutes. This procedure may be repeated from time to time.

*Toxæmia.*—In severe attacks of enteric fever toxæmia is profound, and by the third week nervous symptoms are prominent and circulatory failure is liable to occur.

Cold water should be freely administered by the mouth. The intravenous injection of from 4 to 8 pints of 5 per cent. glucose saline daily, by the drip method, is very beneficial.

Tepid or cold sponging every four hours is a valuable procedure. Immersing the patient in a bath at 85° F. four-hourly is a very effective but a difficult procedure to carry out in private practice. Delirium calls for appropriate drug treatment (see p. 6), and cardio-vascular failure for the intravenous injection of 50 per cent. glucose saline. Cyanosis and dyspnoea are indications for the continuous administration of a mixture of oxygen and carbon dioxide by the nasal catheter.

*Hæmorrhage and Perforation* (see p. 541).—The practitioner must be on the lookout for these serious complications during the third week of the illness. A suitable blood donor should be on call. On the first appearance of blood in the stools or a sudden drop in temperature accompanied by a rising pulse rate, all food and water should be stopped and  $\frac{1}{4}$  gr. (16 mg.) of morphine plus  $\frac{1}{160}$  gr. (0.6 mg.) of atropine sulphate promptly injected. When the effect of the morphine begins to wear off, 5 gr. (0.3 gm.) of Dover's powder may be administered every four hours until the bleeding stops. Should Dover's powder not be well tolerated, 5 minims (0.29 c.c.) of Battley's solution of opium four-hourly should be substituted. In severe or persistent hæmorrhage the motions should be received into tow, the foot of the bed raised on blocks, the lower limbs bandaged from below upwards, extra hot bottles inserted and blood transfusions administered. Preparation such as hæmoplastin or coagulen-ciba are of no value and are no substitute for transfusion.

Nothing should be given by mouth, except water and fragments of ice to suck, until the hæmorrhage has ceased. Feeding may then be resumed by the hourly administration of dessertspoonfuls of glucose lemonade, diluted milk, etc., the amount to be cautiously increased day by day until the intake is again adequate.

If the bowels have not moved, an olive oil enema may be given four days after the hæmorrhage has ceased.

Surgical assistance must be summoned immediately perforation is suspected. Morphine should be withheld until the diagnosis is confirmed.

*Phlebitis.*—Thrombosis of the veins of the lower limbs is a common complication during convalescence. The affected limb is immobilized with

pillows for four weeks, after which period gentle massage and passive movements may be started. The application of hot fomentations will help to relieve the early pain. The use of heparin is contraindicated because of the danger of precipitating hæmorrhage from the bowel.

**Other Complications.**—The pain of cholecystitis can be ameliorated by the local application of hot fomentations and the hypodermic injection of morphine and atropine. Suppurative cholecystitis or perforation of the gall-bladder will necessitate surgical aid.

Suppurative bone lesions must be treated on surgical lines. Material from a periosteal abscess may contain typhoid bacilli, and soiled dressings should be handled with care.

**Convalescence.**—It is advisable to confine the patient to bed for at least fourteen days after the temperature has returned to normal. Relapse is not uncommon. Three consecutive negative cultures for enteric organisms must be obtained at weekly or bi-weekly intervals from stools and urine prior to the release of the patient from isolation. Discharges from bone lesions or other sources will also require to be examined bacteriologically.

The duration of convalescence varies greatly according to the severity of the illness—ranging from one month in a mild attack of paratyphoid B fever to six months or even longer after a severe infection with *Bact. typhosum*. On the whole a longer convalescence is necessary after enteric than after any other acute infection.

**Treatment of Carriers.**—Enteric organisms continue to be excreted in the stools and/or urine for a variable period of time during convalescence.

As was emphasized in the discussion of diphtheria carriers, the condition usually superimposes itself upon some pre-existing chronic condition. In the case of a urinary carrier, a full examination of the urinary tract is desirable, for it is sometimes possible to rectify the abnormality. The faecal carrier state is often associated with chronic cholecystitis and its eradication is not so lightly undertaken. Sulphonamides alone have not proved effective, but in some cases a combination of sulphathiazole and penicillin may be effective. Sulphathiazole is administered orally—for an adult 2.0 gm. four-hourly for seven days. Penicillin is administered systemically at the same time, 15,000,000 units being administered over a period of seven to ten days. There is no doubt that the typhoid group may be inhibited by the action of penicillin, but only in high concentrations. Streptomycin, which has been introduced especially for its effect upon the gram-negative organisms, is still under trial, but the early results are not impressive. The oral administration at three-day intervals of three doses each of 4.0 gm. of soluble iodophthalein as used in the X-ray examination of the gall-bladder has occasionally been successful in clearing the faecal carrier state and the method is worth trying. It is impracticable to isolate the persistent convalescent carrier indefinitely, and the practitioner, when faced with this difficulty, should apply to the local Medical Officer of Health for advice. An individual should not be classified as a chronic carrier until he has been excreting typhoid bacilli for one year. Prior to release from isolation, typhoid carriers must be given detailed written instructions regarding personal hygiene, and must undertake not to engage in any occupation entailing the handling of food. Members of the household to which the carrier returns should be inoculated against enteric fever.



Cholecystectomy will cure 75 per cent. of chronic intestinal carriers, and nephrectomy has proved successful in selected urinary carriers. Operative measures, however, are by no means free from risk and should only be advised after very careful consideration of the patient's physical and environmental condition.

Where typhoid bacilli continue to be excreted from a chronic bone lesion, appropriate surgical measures are usually effective in clearing up the condition.

## ENCEPHALITIS LETHARGICA

(*Epidemic Encephalitis*)

(See p. 862)

## ERYSIPELAS

Erysipelas is a notifiable disease: some local authorities do, in fact, arrange for the treatment of such cases in hospital. The infectivity is, however, slight, and, provided simple aseptic precautions are taken, there is no reason why the patient should not be treated at home.

The general measures to be adopted are similar to those applicable to any other acute infection. Careful nursing is important since the disease frequently attacks elderly patients, often as a complication of some other disease.

**Local Treatment.**—It is doubtful if any type of local treatment has a beneficial effect upon the dermatitis. The assessment of the value of any form of treatment in erysipelas is exceedingly difficult owing to the natural tendency of the disease towards spontaneous cure. Many so-called specific treatments have thus gained a reputation through the observation of their effects in small and uncontrolled series of cases. It is only when large numbers of patients have been treated that the inefficacy of certain methods can be proved. Thus the application of mild antiseptic ointments to the lesion has no value in limiting its spread, while painting the spreading margin with tincture of iodine or with collodion is equally ineffective. Local applications, however, do have a place in the treatment of certain cases owing to their value in relieving pain and oedema. Compresses of carbolic lotion 1 : 60 or 1 : 80, anhydrous magnesium sulphate (50 per cent.) in glycerin, or even simple hot fomentations may be of benefit for this reason, and should always be used in cases of facial involvement where gross oedema is present. In certain cases, too, the desquamation which appears on the site of the lesion, especially when there has been much vesication, gives rise to discomfort. The application of the following salve gives relief: oil of cloves, 1 per cent.; oil of eucalyptus, 5 per cent.; soft paraffin to 100.

**Curative Treatment.**—*Antitoxin.*—As the disease is of streptococcal origin the administration of scarlet fever antitoxin has been advised. The writer has employed this serum both locally and intravenously and has failed to observe any beneficial effect on the toxæmia, pyrexia or the lesion itself.

*Sulphonamides.*—The use of the sulphonamide group of drugs, however, has so greatly hastened recovery that no other form of treatment is, as a rule, required. (For a more detailed reference to these drugs, reference should

be made to p. 71.) Many favourable reports upon their value in the treatment of erysipelas have been published. A critical assessment of over 1,500 cases has shown that a complete cure of the disease can be expected within a period of three to four days.

Sulphanilamide is the drug which should be used. For an adult 6.0 gm. to 9.0 gm. daily should be administered; under the age of five years a daily dose of 3.0 gm. will be found satisfactory. Children tolerate the drug exceedingly well, and, as the disease is often more severe in infancy, relatively large doses may be employed.

In order to maintain an effective concentration of sulphanilamide in the blood, the drugs should be given by mouth at four-hourly intervals, and if a dose be omitted for any reason the subsequent dose should be doubled. Parenteral administration shows no therapeutic advantage over the oral route, and its use should be reserved for critically ill patients first seen late in the disease where it is desired to obtain a high blood concentration in a short time or where intractable vomiting is present. It will rarely be necessary in this disease.

If the drug is used in the suggested doses the lesion will cease to spread within forty-eight hours, and in the majority of cases the temperature will become normal in three or four days. Should the latter not occur, the correctness of the diagnosis should first of all be reviewed; secondly, the presence of some pyogenic complication should be excluded; and thirdly, the question of fever, directly due to the drug, should be considered. Even after the local lesion has subsided the drug may be continued with advantage for a further period of seven days. When this practice is insisted on, recurrence of the disease is unusual.

*Penicillin.*—Penicillin achieves a rapid cure in erysipelas, but in view of the excellent results obtained with sulphanilamide and the ease of its administration the antibiotic is not the treatment of choice. Should some reason prohibit the use of sulphonamides it will be found that the intramuscular injection of 20,000 units four-hourly for a period of five days will give satisfactory results.

Certain symptoms are commonly present which require attention. *Head-ache* is frequently complained of, but is usually relieved by 5 to 15 gr. (0.3 to 0.9 gm.) of acetyl-salicylic acid. *Insomnia*, when present, should be treated early because of its exhausting effect upon the patient and also because it may lead eventually to delirium. 1 to 2 drachms (3.6 to 7.2 c.c.) of syrup of chloral or 5 to 15 gr. (0.3 to 0.9 gm.) of Dover's powder are suitable. *Delirium* in the early stage is not uncommon.  $\frac{1}{4}$  gr. (16 mg.) of morphine tartrate and  $\frac{1}{16}$  gr. (0.6 mg.) of hyoscine hydrobromide should be given and, if necessary, repeated. When a history of alcoholism is obtained it is advisable to continue moderate doses of whisky during the acute stage.

**Treatment of Complications.**—The incidence of complications is exceedingly low if treatment with sulphanilamide is begun early. Inflammation of the associated lymph glands is frequently present, but will usually subside without any local treatment. Should the glands suppurate, simple hot fomentations are helpful. Incision should be delayed until complete coalescence has occurred and fluctuation is definitely present. Healing is then more rapid. Subcutaneous abscesses are not infrequent. Here, again, incision should not be made too early. The abscess frequently underlies the original

erysipelatous lesion and healing is more rapid if its cure has first been established. Acute nephritis, usually of focal type and early in its appearance, rapidly subsides with cure of the local lesion. Since gross failure of renal secretion very rarely occurs if an ample fluid intake is insisted on, there is no contraindication to the use of sulphanilamide. Septicæmia is now rarely seen to develop in the treated case. Its presence at the outset calls for an intensive course of sulphonamide, and the employment of such additional methods of treatment as this serious condition demands.

## GLANDULAR FEVER

### *(Infective Mononucleosis)*

Epidemics of this acute infectious disease of unknown ætiology have of recent years occurred in various schools and institutions, and sporadic cases are not uncommon among the general population. Whilst susceptibility to the disease appears to be almost universal, the degree of infectivity is not high. For example, cases of glandular fever can be treated in a mixed ward with no ill results. The method by which the disease is spread is unknown, but it may be by droplet infection. The incubation period lies usually between five and fifteen days. Fever accompanied by acute enlargement of the lymph glands, particularly of the neck, is the form of the disease commonly met with in children. Febrile and anginose types occur in young adults. A mononuclear leucocytosis is characteristic of the disease. The Paul-Bunnell sheep-cell agglutination test has proved a valuable aid to diagnosis; agglutination in a titre of 1:160 or higher may be regarded as diagnostic. The bacteriologist should be informed if horse serum has been administered, since this gives rise to false positive results.

Glandular fever, or infective mononucleosis as it is sometimes called, is not a notifiable disease.

**Preventive Treatment.**—There is no specific method of prophylaxis against glandular fever.

Providing reasonable precautions are taken and the patient isolated, there is little chance of other members of the household becoming infected. Contact children should be kept under observation for a period of three weeks, dating from the last contact, but need not be kept away from school. In residential schools the isolation of contacts usually proves ineffectual in limiting the spread of the disease.

**Curative Treatment.**—There is no therapeutic measure yet available which will cut short the disease. The treatment of glandular fever is purely symptomatic.

**General Management.**—The patient should be confined to bed and kept there until the temperature has been normal for one week and the glandular swelling markedly diminished. The diet is limited to fluids and soft solids during the febrile stage of the illness, and water freely administered. Hot fomentations may be applied to the neck if the swollen glands are painful. The anginose type in adults simulates diphtheria, but the faucial exudate does not respond to treatment with diphtheria antitoxin. In most cases the secondarily infecting organisms are susceptible to the action of penicillin. Although the sucking of pastilles or lozenges containing the antibiotic is advised, it is generally wiser to administer penicillin systemically. Three or four days of treatment usually suffices.

The febrile type with high and prolonged pyrexia, lasting several weeks, requires to be treated on the same lines as a case of enteric fever.

Whilst little is known regarding infectivity, it is probably a wise precaution to disinfect the secretions from the upper respiratory tract.

Meningitis, epistaxis, hæmaturia and conjunctivitis are occasional complications.

**Convalescence.**—Recrudescences are liable to occur. Even after mild attacks anæmia and slight debility may persist for several months and the patient should return gradually to normal life. A change of air is definitely beneficial, and 45 gr. (2·7 gm.) daily of Blaud's pill or 90 gr. (5·4 gm.) daily of iron and ammonium citrate should be prescribed.

## INFLUENZA

Influenza is a virus infection; but it is probable that a number of closely related viruses give rise to a similar clinical syndrome. Two main viruses (Virus A and Virus B) have now been isolated from nasopharyngeal washings of patients in epidemic periods, Virus A being associated as a rule with more widespread and severe epidemics. The actual isolation of the virus is not the only method of exact diagnosis; antibodies develop in the blood serum during an attack and these may be measured by the Hirst test. For diagnostic purposes, two specimens of blood are required; one in the early stage of illness, the other about one week later. A two- to four-fold increase in antibodies is regarded as evidence that the individual has passed through an actual infection.

The clinical differentiation of cases into groups according to signs and symptoms has been attempted with a view to correlating these with the causal agent, but so far this has not proved of value. The importance of the disease lies partly in its ability to spread rapidly from person to person and thus to cause widespread outbreaks; but also in the danger of secondary bacterial invasion of the lungs. The bacteria responsible vary from time to time, but staphylococci, streptococci, *H. influenza* and *K. friedländeri* are the most important. The sharp rise in the incidence of pneumonia which so frequently occurs at the end of December and beginning of January is almost certainly related to the prevalence of influenza at this time with its quantum of secondary broncho-pneumonia.

The incubation period is short—1 to 2 days—and the disease is only notifiable when complicated by pneumonia.

**Prevention and Epidemiological Control.**—There is no method whereby the spread of infection can be prevented. Free ventilation and avoidance of crowds are clearly advisable, but since many individuals suffering from minor degrees of illness continue with their daily work, the virus is constantly present in crowded trains, trams and buses, and the avoidance of contact is virtually impossible.

Specific prevention by the use of virus vaccines has now been extensively investigated, but although encouraging, the results are by no means clear-cut. Two methods have been tried. First a formolised vaccine suspension may be used. This is administered by intramuscular injection on two occasions, one month apart, each dose being 1·0 c.c. Such injections cause a rise in serum antibodies. The second method is an instillation of live attenuated

virus suspension into the nose in the belief that the formation of local resistance is an important factor. Here again a rise of serum antibodies can be observed. Unfortunately the resulting immunity to both methods is not of long duration, but when carried out just before an epidemic the subsequent attack rate in the inoculated has been reduced.

The so-called "common cold vaccines" have not the slightest effect upon the incidence of upper respiratory tract infection. There is no evidence that mixed vaccines of the common secondary invaders have any effect in reducing the complication rate of influenza.

**Curative Treatment.—General Management.**—Immediately influenza is suspected the patient must be isolated and confined to bed in a freely ventilated room. Isolation should be maintained until the temperature has returned to normal. There is no specific serum or drug treatment of proven value for influenza, so that the main dependence is on efficient nursing and treatment of symptoms (see general management of fevers, p. 2). The nursing features that require emphasis are the hygiene of the mouth, nose, eyes and skin. Where there is nasal or bronchial discharge, paper handkerchiefs are to be preferred which can be burnt as used. Daily bed baths are a comfort to the patient, and indeed when the temperature is high a sponge-down is often followed by a refreshing sleep. For the relief of pain, aspirin and Dover's powder will usually suffice; when there is complaint of sore throat the aspirin should be slowly dissolved in the saliva and gradually swallowed, when it often has a local analgesic effect. Troublesome cough is best relieved by the administration of a sedative such as codeine. Cyanosis usually indicates the presence of a pulmonary complication and oxygen is indicated.

**Sulphonamides and Penicillin.**—Sulphonamides are often used prophylactically. In view of the uncomplicated course in so many of the cases it is difficult to evaluate the results. In the mild case, such a method of prophylaxis is not advised, but if used the dosage should be of the same scale as in treatment. Pneumonia will often be suspected rather than diagnosed, for the physical signs in the chest are seldom typical of consolidation. The response of influenzal pneumonias to chemotherapy is less dramatic than that of the pneumococcal variety, but penicillin should be started at once on the appearance of suspicious symptoms. High dosage of penicillin should be given (0.5 mega units per day for the first two to three days). With streptococcal or staphylococcal infections, lung abscess or empyema is a real possibility and there should be no hesitation in aspirating the chest. (Because of the likelihood of a staphylococcal infection, sulphadiazine is the sulphonamide of choice in influenzal cases.) Pneumonia complicating influenza advances with great rapidity; even within 24-48 hours, a patient may be overwhelmed by a widespread pulmonary infection. Time is thus of importance, for the value of chemotherapy may well be vitiated by tardy and cautious administration. When pneumonia is suspected, there should be no delay in starting treatment with sulphadiazine and penicillin.

**Other Complications.**—Pyogenic complications may arise in the paranasal sinuses or middle ear. In many cases bacteriological examination shows the infecting organism to be penicillin sensitive, and the use of the antibiotic in such cases gives rapid relief. Myocarditis must always be borne in mind, especially in the older patient.

**Convalescence.**—The importance of an adequate period of convalescence

after influenza must be impressed upon the patient. Owing to the toxic effect of influenza on the myocardium it is advisable to keep even the mildest case in bed for at least three days after the temperature has settled. This applies particularly to those over the age of 35 years. In more severe attacks this period should be extended to one to two weeks. The response of the heart to increased exertion must be carefully watched, and further rest enforced if this be unsatisfactory. Fresh air, sunlight, ample good food and exercise short of fatigue will hasten recovery. A change of surroundings is very beneficial, particularly to patients suffering from the characteristic mental depression or residual tracheitis. Cough due to tracheitis is sometimes very persistent, but is usually relieved to some extent by the administration of 1-drachm doses thrice daily of either elixir diamorphinæ et terpini cum apomorphina or syrup of codeine. Infected nasal sinuses may be the exciting factor and should receive appropriate treatment.

Before permitting the patient to resume work the practitioner should satisfy himself by a careful clinical examination, particularly of the cardiovascular, respiratory and nervous systems, that recovery is complete.

## MEASLES

(*Morbilli*)

Measles is one of the most important and most highly infectious diseases of childhood. Owing to the risk of a complicating broncho-pneumonia it is a particularly serious infection in children under three years of age. The causal agent, a filterable virus, is commonly spread by direct contact (droplet infection), particularly during the catarrhal stage of the illness, a stage at which measles is seldom diagnosed. Except for those who have previously suffered from the disease, susceptibility to measles appears to be practically universal. During an epidemic a small proportion of exposed susceptible children may, however, as the result of a process of latent immunization, either escape the disease entirely or suffer from it in a highly modified form. The incubation period is usually from nine to eleven days, but may vary from seven to fourteen days.

In certain areas the first case of measles occurring in a household has to be notified to the Medical Officer of Health. Otherwise the disease is not notifiable.

**Preventive Treatment.**—*Passive Immunization.*—An attack of measles can be prevented or modified by the intramuscular injection of an appropriate dose of one or other of the following preparations, namely: (1) human convalescent serum; (2) the serum of adults who have previously suffered from measles; (3) immune globulin (human placental extract); (4) Cohn's gamma-globulin. As the supply of human convalescent serum is necessarily limited, its use should be reserved for the passive immunization of children under four years of age. The newer gamma-globulin is not yet widely available but has an effect equal to convalescent measles serum.

*Certain progressive Sanitary Authorities have arranged for the collection and issue to practitioners of convalescent or adult measles serum. Placental extract is obtainable commercially.*

Except in an ailing or weakly child, or in a child under three years of

age, the aim should be to attenuate rather than to prevent an attack of measles. Such a procedure may enable the child to gain a lasting immunity. In hospitals, sanatoria or orphanages it is advisable to attempt complete protection as soon after exposure as possible.

The dose of the various prophylactic preparations suitable for a child under five years of age is set out in the following table. Owing to variations in the antibody content of human serum, complete protection cannot, however, always be relied upon to follow the administration of the dosage indicated.

**DOSAGE OF MEASLES PROPHYLACTIC PREPARATIONS**

	Day of Exposure.	Convalescent Serum.	Adult Serum.	Immune Globulin. (Placental Extract.)	Gamma-globulin.
Complete Protection.	First to Fourth.	5.0 c.c.	20 c.c.	8 c.c.	0.1 c.c. per lb. body-weight.
Attenuation .	First to Fourth.	2.5 c.c.	10 c.c.	4 c.c.	
	Fifth to Eighth.	5.0 c.c.	20 c.c.	10 c.c.	

Although placental extract has the advantage of being readily obtained, mild systemic reactions not uncommonly follow its injection, and on rare occasions even severe and alarming collapse has been noted.

The practice of injecting whole blood from a parent or friend is not advised on account of the possibility of inducing Rh. sensitization.

*General Measures.*—Contacts who have not previously suffered from measles are usually excluded from school for three weeks from the date of onset of the last case in the house. Forbes is of the opinion that home contacts should continue to attend school, unless under exceptional circumstances, provided they are inspected daily by the school nursing staff, or by teachers trained to recognize the early symptoms of measles. This procedure, he maintains, would lead to early diagnosis and prompt isolation, and would ensure proper medical care and nursing from the onset of the attack. No restrictions need be applied to children who have previously suffered from measles. When measles is prevalent susceptible children should not attend parties, the cinema or other gatherings.

The view widely held among the public that, as a child will probably contract measles some time, the sooner it passes through an attack the better, cannot be too strongly condemned. Every precaution should be taken to prevent the exposure of young children to measles.

*Curative Treatment.*—*Serum.*—There is no specific of value in the treatment of measles. The intramuscular injection of human convalescent serum or of gamma-globulin has no demonstrable clinical effect.

*General Management.*—Immediately measles is suspected, the child must be isolated and confined to bed in a freely ventilated yet warm (60° to 65° F.) room. Isolation not only prevents further spread but protects the patient,

for the real danger of measles lies in the complications arising from invasion with such organisms as *S. pyogenes*, the pneumococcus and *H. influenzae*, so that contact with adults and strangers should be avoided. Although in some cases the patient may be harbouring these organisms in the upper respiratory tract prior to the onset of measles, in others infection arises through droplet spread from individuals in the patient's environment. Under no circumstances should attendants or visitors suffering from acute or chronic catarrhal infection be allowed into the sickroom unless efficiently masked. The fewer visitors the patient sees the better.

Discharges from the mouth, nose and eyes should be collected on rags or paper handkerchiefs and promptly burnt.

The bed should be placed so that the patient does not face the light. Excess of bedclothes is a common fault; a sheet and one or, at most, two layers of blanket is ample. The patient should wear a single cotton or flannel nightgown and be kept warm by hot-water bottles. The whole skin surface should be sponged with soap and warm water once daily. Milk of magnesia or other mild aperient may be administered as indications arise.

The management of measles does not differ from that of any febrile patient and reference should be made to p. 2. Particular attention must be paid to the hygiene of the mouth, nose, eyes and skin, for the damage done there by virus will open up pathways for more serious bacterial invasion. The most irritating symptom is the repeated harsh cough. Inhalations of steam with Friar's balsam often relieve this and are particularly good with children; in adults heroin or codeine, in the form of the glycerines, by diminishing the cough reflex, is the better treatment.

**Complications.—Sulphonamide Prophylaxis.**—The danger of secondary bacterial invasion in measles is of short duration for, once the mucous membranes are healed, the risk diminishes. Provided the patient is being properly isolated and access of visitors prevented, there is no need for specific prophylaxis, and chemotherapy should only be used when the ordinary therapeutic indications for it are present; but where several children are nursed together the danger of cross-infection from one to the other is greatly increased and chemoprophylaxis is worth employing. Sulphathiazole or sulphadiazine should be used in therapeutic dosage until the rash has faded or for 48 hours after the subsidence of the fever. The use of sulphonamides should not lull the practitioner into a sense of false security. Complications may yet arise; and otitis media in particular should be carefully looked for. When *otitis media* occurs, bacteriological examination of the pus is very desirable. Penicillin, given systemically, is of great benefit when the organism is sensitive to it; in very young children, however, *B. coli* may be one of the infective organisms and may inhibit the value of the antibiotic. In such cases, careful toilet of the ear, twice daily, is desirable. If the discharge is profuse and thick, gentle douching is helpful. Instillation of powders (boracic and iodine is good) or of mild antiseptics is worthy of trial.

**Broncho-pneumonia.**—Broncho-pneumonia is the most serious complication. In most cases the organism is responsive to sulphadiazine or sulphathiazole but penicillin may be used in addition in severe cases.

A mild degree of *laryngitis* is a common early symptom in measles. As a general rule laryngitis during the catarrhal stage is almost certainly coccal in origin and will improve as the rash emerges. Laryngitis that arises *after*



the appearance of the rash is *almost certainly diphtheritic* and should be treated as such. In addition to diphtheria antitoxin, penicillin should be administered. The subsequent treatment of the condition is on the lines described in the chapter on Diphtheria (see p. 16).

In the same way, gastro-enteritis may be expected during the catarrhal or early rash stage as a natural part of the disease; its occurrence, thereafter, should raise the immediate suspicion of dysentery.

The appearance of corneal ulceration calls for dilatation of the pupil, either by atropine drops or ointment ( $\frac{1}{4}$  per cent.) and the use of 10 per cent. mild silver protein (B.P.) drops thrice daily. No time should be lost in obtaining the advice of an ophthalmologist.

**Convalescence.**—In an uncomplicated case the child may be allowed out of bed about the tenth to twelfth day from the onset of the disease, and out of isolation on the fourteenth day. Plenty of good wholesome food and exercise in the open air will hasten convalescence. A holiday at the seaside or country is very beneficial, particularly to cases with residual pulmonary catarrh.

## MUMPS

(*Epidemic Parotitis*)

The infective agent in mumps is a filterable virus which is present in the saliva during the acute stage of the illness. The disease is commonly spread by direct contact (droplet infection), and possibly by articles recently contaminated with infective saliva. Infectivity probably persists from the onset of the first symptom until the swelling of the salivary glands has subsided. The incubation period varies from twelve to twenty-six days, but usually lies between seventeen and twenty-one days.

Whilst the parotid is the gland most frequently involved, it is well to remember that the submaxillary or sublingual salivary glands may be exclusively affected and that abortive attacks of mumps, owing to the lack of facial deformity, may readily be missed. The occurrence of a lymphocytosis is of some diagnostic value.

Mumps is not a notifiable disease.

**Preventive Treatment.**—*Specific Prophylaxis.*—The intramuscular injection of 10 c.c. of serum from a mumps convalescent has been successfully employed as a prophylactic. It is doubtful if the method is worth while in such a habitually mild disease. Indeed, no attempt should ever be made to avoid mumps occurring in a child under 12 years; complications (especially orchitis) do not arise and the risk of an adult attack is thus diminished.

**General Measures.**—The patient must be promptly isolated. The quarantine period for mumps contacts is twenty-six days, but where the date of exposure is definitely known, an exposed child may safely attend school for the first ten days of this period. In actual practice, providing a contact is examined daily and isolated on the first suspicion of illness, exclusion of contacts from school in the case of a mild infection like mumps seems unnecessary. A child who has previously suffered from the disease may, for practical purposes, be regarded as immune and need undergo no restrictions. Adult contacts may continue their business activities.

**Curative Treatment.**—*General Management.*—There is no specific treatment for mumps.

The patient should be confined to bed until the swelling subsides. There is no evidence that rest in bed prevents the occurrence of orchitis and mild cases even in adults may be allowed up by the fifth or sixth day. Difficulty in opening the mouth and pain on mastication are indications for the restriction of the diet to fluids and soft solids.

Hot dry cotton-wool or hot fomentations applied to the swollen glands will help to relieve pain and local discomfort.

The mouth should be washed out with a 1 : 5,000 solution of permanganate of potash or other mild antiseptic preparation four times daily.

**Treatment of Complications.**—Orchitis usually develops when the parotid swelling is at its height and may be expected in approximately 20 per cent. of males above the age of puberty. The scrotum should be surrounded with hot dry cotton-wool and the inflamed parts supported either by a pillow placed between the thighs or by a suspensory bandage. The bowels should be freely opened by the administration of  $\frac{1}{2}$  to 1 oz. of magnesium sulphate.

Symptoms of gastric disturbance are usually due to pancreatitis. A hot bag or hot fomentations applied to the site of the pain, with limitation of food and the exclusion of fat from the diet, will give relief. If the pain be severe,  $\frac{1}{4}$  gr. (16 mg.) of morphine may be injected hypodermically.

Meningeal symptoms are liable to be met with in some epidemics, and, if severe, should be relieved by repeated lumbar puncture.

There is no effective treatment for acute labyrinthitis, which is fortunately a very rare complication.

**Convalescence.**—Convalescence is usually rapid. Isolation of the patient should be continued for one week after the parotid swelling has subsided. The minimum isolation period is fourteen days. To diminish the risk of orchitis, adult patients should avoid erotic excitement, cycling or riding for at least one month after recovery.

## POLIOMYELITIS

### (Infantile Paralysis)

The incidence of paralytic cases gives a very erroneous impression of the actual prevalence of poliomyelitis. The presence of neutralizing antibodies in the blood serum of from 50 to 60 per cent. of the adult population indicates that a large proportion of urban dwellers have suffered from an unrecognized or abortive attack of poliomyelitis. The exact mode of transmission is not yet clearly established, but recent work has emphasized the importance of faecal carriage, and has placed poliomyelitis in the same category as enteric fever as regards mode of transference. This work must be regarded as still *sub iudice*.

Carriers and unrecognized or abortive cases play a very important part in the spread of this serious disease.

The duration of infectivity is unknown. The virus has been isolated from the nasopharynx during the third week of convalescence, and in one case as late as four months after the onset. The virus is excreted in the faeces.

The incubation period appears to vary from five to seventeen days, the average period being nine to twelve days.

Poliomyelitis, including polioencephalitis, is a notifiable disease,

**Prevention and Epidemiological Control.**—*Specific Prophylaxis.*—Human convalescent or adult serum has been extensively used as a prophylactic against poliomyelitis, but the results have been disappointing. If it be desired to give the method a trial, 20 c.c. of human convalescent serum may be injected intramuscularly.

Attempts to produce an active immunity against poliomyelitis by means of vaccines have not so far proved successful.

*General Measures.*—The probability that the virus of poliomyelitis may be more or less widely distributed among the contacts, even by the time the first clinical case is recognized, raises difficult problems in control.

On the occurrence of a case of poliomyelitis in a household the patient must be promptly and effectively isolated. Children who have been in contact with the patient are strictly quarantined and kept under medical surveillance for a period of three weeks from the date of last contact. Adult contacts may continue their occupation providing it does not entail mixing with children as in the case of nurses and school-teachers. They should, however, abstain from all social activities for three weeks from the date of last contact; kissing or playing with young children must be strictly forbidden.

A contact who suffers from a febrile catarrh or other symptoms suggestive of an abortive attack of poliomyelitis should be strictly isolated until recovery ensues.

The importance of free ventilation cannot be too strongly emphasized. Contacts should spend as much time in the open air as possible. Children should not sleep together in the same bed. The common use of handkerchiefs must be discouraged.

The routine use of an antiseptic gargle and nasal douche or spray is of very doubtful prophylactic value. Warm normal saline may, if desired, be sniffed up the nostrils twice or thrice daily, and returned through the mouth.

The prevention of epidemic spread of poliomyelitis in residential schools and institutions is a problem for the local Medical Officer of Health. Adequate spacing of beds in dormitories and free ventilation are of paramount importance. If either closure of an infected residential school is decided upon or the opportunity of removing exposed susceptible pupils is offered to parents (which offer should be accepted), then the pupil must on return home be strictly isolated from other children and kept under medical supervision for three weeks.

Whilst an epidemic prevails, young children should not be permitted to enter any house wherein there is a case of poliomyelitis, and all gatherings of children should be avoided. Closure of day schools may have to be considered.

As tonsillectomy has on many occasions transformed a mild subclinical poliomyelitic infection into a fatal bulbar type of the disease, this operation should, if possible, be postponed until epidemic prevalence has subsided.

**Curative Treatment.**—*Serum Treatment.*—Convalescent serum has no effect upon the course of poliomyelitis, for by the time a diagnosis has been made the virus is in the nerve cells and beyond the reach of antibody.

*General Management.*—*Pre-paralytic Stage.*—During epidemic prevalence the occurrence of such symptoms as fever, headache, pain in the back, stiffness of the neck, drowsiness with irritability and weakness should lead to

immediate enforcement of the following measures and prompt examination of the cerebrospinal fluid.

Absolute rest, quiet surroundings, the minimum of handling and the relief of pain and insomnia are the essentials in the treatment of the pre-paralytic stage of acute poliomyelitis. If trained day and night nurses cannot be obtained, the patient should be transferred to hospital.

Isolation should be strictly enforced and visitors discouraged. Discharges from the nose and throat must be carefully collected on rags or paper handkerchiefs, which are promptly burnt. The urine and stools may be infective and require to be disinfected.

Hyperæsthesia and fear of pain on handling are usually prominent symptoms. The painful limb or muscles should be wrapped in hot dry cotton-wool and kept warm by extra hot bottles. Repeated simple hot fomentations often bring immediate relief. When the lower limbs are, or may be, involved a cradle must be employed. Aspirin in doses of 2 to 10 gr. (0.12 to 0.6 gm.) every four hours will help to relieve pain. Chloral and bromide should be prescribed for restlessness or insomnia. Otherwise the treatment of the case is on general lines.

*Paralytic Stage.*—When paralysis is evident, the extent of muscular involvement must be carefully assessed and the affected limbs kept in the appropriate position by means of sand-bags or light splints. Paralysed legs should be kept extended, slightly flexed at the knees, abducted and rotated in with the feet kept at right angles to the legs; a small pillow should be inserted beneath the knees and the child kept flat. In the case of paralysis of the deltoid muscle the arm should be abducted to a right angle with the body. Involvement of the muscles of the back necessitates a strictly supine and straight position in bed until such time as a proper spinal support can be applied. In pharyngeal paralysis, the foot of the bed should be raised eighteen inches, secretions aspirated from the pharynx at regular intervals by a soft rubber catheter, and food administered by the nasal tube, supplemented if necessary by intravenous or rectal glucose salines. The mechanical respirator affords the only effective therapeutic measure in cases suffering from paralysis of the respiratory muscles. When all muscle tenderness has disappeared, plaster cases and splints should be applied under the guidance of an orthopædic surgeon, who should, in fact, be called upon to supervise the case from the onset of paralysis. The limb should not be encased in plaster but should lie in plaster "shells" so that daily gentle massage and passive movements of the affected limbs may be supplemented by the local application of radiant heat. Treatment in the open air is of great value. After an isolation period of six weeks, arrangements should be made to secure continued orthopædic supervision and treatment, preferably by transfer of the patient to an orthopædic hospital. It should be emphasized that careful attention to the paralysed limbs during this first six weeks is of paramount importance and makes a great contribution to the ultimate complete recovery of the patient.

## PSITTACOSIS

Human infection with the virus of psittacosis usually arises through contact with diseased parrots, budgerigars or other members of the parrot family, but the disease may also be contracted from infected canaries,

finches or fulmar petrels. The bird may show signs of illness. On the other hand, apparently healthy home-bred birds may carry the virus and prove to be a very real danger. The filterable virus is excreted in the bird's droppings, and the portal of infection in man is probably the respiratory tract. Human case to case infection has been suspected but not proven.

The duration of the incubation period is uncertain, but may be seven days or longer.

Psittacosis is not a notifiable disease.

An acute febrile illness with combined typhoidal and pneumonic symptoms occurring in a person who has to do with parrots, etc., is probably psittacosis. The diagnosis can be confirmed either by the isolation of the virus from the blood or sputum, or by the complement fixation test. An attempt should be made to demonstrate psittacosis virus in the suspected bird even though the latter may appear healthy.

**Prevention and Control.**—As a result of the epidemic of psittacosis in this country in 1930, the immigration of birds of the parrot family was strictly controlled. Unfortunately, this policy has failed to banish the human disease. The simple and obvious method of prevention rests with the public, who if they do not wish to run the risk of psittacosis should not keep these birds in their homes.

Actually the risk of contracting the disease from birds that have been in a household for many months or years is negligible, but newly acquired birds should be suspect.

Persons owning these pets should (1) avoid fondling and petting the birds; (2) protect food and water from fouling by the birds; and (3) keep the cage thoroughly clean. An ailing bird of little monetary value should be killed and burnt; if of value, it should be isolated and laboratory aid enlisted to arrive at a diagnosis. Extreme care must be taken in handling and disinfecting all articles with which the bird has come in contact.

**Curative Treatment.**—There is no effective specific treatment for psittacosis.

Treatment is purely symptomatic and the general management of the case is on the lines recommended for enteric fever and pneumonia.

Although isolation need not be enforced, it is probably wise to regard the patient as potentially infective. Sputum, urine and stools should be disinfected.

## RUBELLA

*(German Measles)*

Probably a virus infection, rubella is spread by direct contact and, possibly, by fomites. There is no information available regarding the conveyance of infection by carriers.

Infectivity appears to be limited to the prodromal and eruptive stages of the illness.

The incubation period is usually from fourteen to eighteen days, but may vary from twelve to twenty-one days.

Rubella is not a notifiable disease.

**Preventive Treatment.**—There is no specific method of prophylaxis against rubella.

Contact children who have not had the disease should be excluded from school for three weeks from the date of last exposure to the patient. When the date of exposure to infection is definitely known, absence from school may safely be curtailed to the period from the eleventh to the twenty-first day inclusive. If quarantine is not practised, school contacts must be inspected daily, and promptly isolated on the appearance of slight catarrh or swollen cervical glands. Apart from nurses, school-teachers, etc., adults who have been in contact with a case of rubella may continue their business activities.

Reference must be made to the recent observation that rubella in the first three to four months of pregnancy may induce changes in the foetus which may be born with congenital defects. The common abnormalities reported have been congenital cataracts, deafness and cardiac defects. That there is a connection between the two seems now beyond doubt; how frequently the disease does cause defects, however, is not yet known, although published figures would suggest that it is less than 1:10. Although induced abortion has been advised it is felt that in the light of our present knowledge such a course exaggerates the danger.

**Curative Treatment.**—Treatment is purely symptomatic. The patient should remain in bed until the temperature has subsided and the rash faded. The illness is usually so mild that the patient can be kept on an ordinary diet and no special treatment is required.

Complications are rare.

An isolation period of one week from the appearance of the rash is ample.

## SCARLET FEVER

(*Scarlatina*)

Scarlet fever results from infection usually of the throat with *S. pyogenes* and, to occur, necessitates two prerequisites. First, the streptococcus must be able to produce a specific toxin; and second, the host attacked must be susceptible to that toxin. The typical rash (and perhaps some of the other signs) is produced by this toxin, which is therefore often referred to as the erythrogenic toxin. Since there may be wide variation both in the toxigenicity and in the host-susceptibility, there is great variation in the severity of the clinical syndrome so that many mild cases occur. These are liable to be missed and are a potent source of spread of infection. Individuals who have become immune to the toxin are not immune to streptococcal infection. When they are infected, a streptococcal tonsillitis may occur, and such persons, perhaps even more than carriers, play an important part in the spread of the disease and render control virtually impossible.

Although infection therefore is very commonly from "missed case" to case, the contamination of animate or inanimate materials by streptococcal discharges is also of importance. Infected milk is a common cause of epidemics. Dust also may bear streptococci, and measures to control dust form an important aspect of control.

After recovery, cases both of scarlet fever and of tonsillitis may continue to carry streptococci in the throat or nose. Upon this fact is dependent the duration of infectivity. Since the number of carriers normally present in the community is large, there is no justification for continuing isolation

because of positive throat swabs unless the individual's occupation makes it especially dangerous for others. Only nurses (especially midwives), teachers and individuals associated with a milk supply should be subjected to detailed bacteriological examination.

Scarlet fever has a short incubation period—from two to five days—and is a notifiable disease.

**Prevention and Control.**—*The Dick Test.*—This test, which is analogous to the Schick test (*q.v.*), measures the capacity of the individual to neutralize the erythrogenic toxin. The material used is commonly designated Dick toxin, and 0.2 c.c. of this is injected intradermally into one forearm at the same time as a control injection of like amount is injected into the other. The test must be read much earlier than the Schick test and twelve to eighteen hours is the usual time interval. Readings similar to those of the Schick test are made—a positive result (an area of erythema of 1 cm. or more) indicating susceptibility to scarlet fever. Pseudo-positive reactions are uncommon in children.

Most infants remain Dick negative until the age of about six months. By the end of the first year 90-95 per cent. have become Dick positive, and this proportion gradually falls with each succeeding age-group so that by the age of 18-20 years only 20-25 per cent. of the population remains Dick positive. It must be appreciated that the result of the Dick test gives no indication of the individual's susceptibility to streptococcal infection but merely of his capacity to cope with the toxin.

*Active Immunization.*—At least 90 per cent. of Dick positive reactors can be rendered Dick negative by the subcutaneous injection at weekly intervals of 500, 2,000, 8,000, 25,000 and 50,000 skin-test doses of sterile scarlatinal toxin. A Dick test should be performed four weeks after completion of the course. The immunity so attained, which is purely anti-toxic, will in the majority of individuals last for years, but cannot be relied upon to prevent upper respiratory tract infections with the scarlatinal streptococcus. A modified course of 500, 3,000, 12,000 and 30,000 skin-test doses of toxin, administered at weekly intervals, will in most cases produce a satisfactory but shorter lived immunity.

Unfortunately, the immunizing injections are liable to give rise to unpleasant but not serious reactions. These occur most commonly with the fourth injection, and in particularly susceptible individuals a reduction in its amount and the addition of a further injection at the end may prove helpful.

Although active immunization is the most effective procedure in the prevention of epidemics of scarlet fever in residential schools and institutions, this method of prophylaxis is unsuitable for general application during the present mild phase of scarlet fever.

Where one member of a household has previously died from scarlet fever, or where there is a family history of undue susceptibility to the disease, the practitioner should attempt to immunize the remaining susceptible members of the family.

*Passive Immunization.*—The injection of a dose of scarlet fever anti-toxin as a means of procuring passive immunity has little to recommend it. As has already been pointed out, the subsequent immunity is only partial and other forms of streptococcal infection may still occur. In a closed community this will mean that infection is kept "alive," and when passive immunity has waned, further cases of scarlet fever may arise.

*Sulphonamides.*—Sulphanilamide has some effect in inhibiting streptococcal infection. It is the least toxic of the sulphonamides and in the face of an epidemic in a residential community its administration in a therapeutic scale of dosage is worthy of trial.

*Penicillin.*—Systemic penicillin will clear streptococci from the throat and thus prevent spread of infection. With healthy individuals the need for four-hourly injections of the material will not commend its use. In ward outbreaks in hospital, however, it undoubtedly limits the spread of the organism, and in such conditions with the patient more under control the systemic administration of 100,000 units daily for five days will usually suffice to break the chain of infection.

*General Measures.*—The patient must be promptly and effectively isolated. Contact children should be excluded from school for one week after removal of the patient to hospital. When the patient is treated at home, the local health authority may insist on the remaining susceptible children of the household being kept away from school throughout the period of treatment. Where arrangements can be made for susceptible home contacts to live with adult relatives, loss of school time can be materially diminished.

A quarantine period of at least one week must be strictly enforced in the case of adult contacts whose occupation entails the handling of milk or other food substances or close contact with children. Unless the serological type which infected the first case is known, the swabbing of contacts should not be encouraged. If typing can be carried out the search has some precision and is then worth doing. About 20 per cent. of the normal population may be expected to show hæmolytic streptococci in nose or throat.

If an epidemic of scarlet fever is to be stamped out in a residential school or institution, typing becomes essential, so that cases of hæmolytic streptococcal tonsillo-pharyngitis and carriers of the specific organism may be isolated. Bacteriological assistance must be employed as a routine measure.

The practical problems involved in the effective control of scarlet fever have still to be solved.

*Curative Treatment.*—*Serum Treatment.*—The early administration of scarlet fever (streptococcus) antitoxin rapidly alleviates the toxæmic symptoms, and thus renders the patient more comfortable.

Antitoxin may be expected to alleviate only those signs and symptoms due to the specific toxin. Thus the fever abates rapidly, often by crisis; the rash fades within 12-24 hours and desquamation is thereby reduced in extent; the œdema of the throat and the associated lymph glands is greatly diminished; and there is a rapid amelioration of the patient's general condition. But although early antitoxin administration by producing these results may be expected to effect some diminution in the incidence of these complications due to streptococcal invasion, they will not be completely eliminated. Indeed, once invasive tendencies are apparent, serum seems to have little effect. On the other hand, in the toxic type of case such a method of treatment may prove life saving.

For the present mild form of scarlet fever the administration of antitoxin is not always necessary. The best guide is the appearance of the rash; the brighter and more intense it is the greater the need for antitoxin. Such a rash is usually associated with a high fever (over 101° F.), œdema of the fauces and early cervical adenitis, and the presence of these are further



indications for serum treatment. Needless to say, once the rash has faded, serum need not be administered—for the purpose for which it is intended, namely, the supply of antibodies, has already been achieved by the patient. The usual dose is from 3,000 to 10,000 units contained in 3-5 c.c. of refined antitoxin. The intramuscular route will suffice for the moderately severe case, but in severe or toxic cases the intravenous or intraperitoneal route should always be used.

*Sulphonamides.*—The sulphonamides do not exert any appreciable effect on the initial toxæmic symptoms of the disease. When administered immediately on the appearance of an early catarrhal otitis media, they may have some effect in inhibiting further extension.

*Penicillin.*—Although, like sulphonamides, penicillin cannot have any effect upon the toxæmic element of the infection, it has a valuable place in the management of scarlet fever. The sulphonamides suffer from the fact that streptococcal invasion is so frequently followed by pus formation; and in the presence of pus, sulphonamide activity is diminished. Penicillin, on the other hand, is effective even when pus is present. It has a particular place in the treatment of the “septic” type of infection; where there is infection of the paranasal air cells or where the middle ear is infected. As a general rule it may be accepted that these complications are streptococcal and treatment may therefore be started at once, but nevertheless specimens should be taken for bacteriological examination and the etiological agent ascertained precisely.

The antibiotic should be given systemically; the effects of local treatment are capricious. In severe infections doses of 0.5 mega units in the 24 hours should be used in starting treatment.

*General Management.*—Where housing conditions are satisfactory, mild and even moderate cases should be treated at home; secondary complications are thereby reduced.

The administration of Dover's powder with aspirin will help to allay headache, insomnia and general discomfort.

In young children mild angina requires no local treatment. In older patients the throat may be sprayed with warm saline or warm  $\frac{1}{2}$  per cent. solution of bicarbonate of soda. A grossly inflamed, dirty or ulcerated throat should first be sprayed with hydrogen peroxide diluted with two parts of warm water, and then freely irrigated with hot normal saline solution to which  $\frac{1}{2}$  per cent. phenol may be added. The treatment may be repeated every two to four hours. Steam inhalations with or without the addition of Friar's balsam are sometimes appreciated, and sucking fragments of ice helps to relieve pain and diminish swelling.

Young children suffering from septic scarlet fever are very difficult to handle, and in such cases, even though the throat be grossly inflamed, it is wiser to limit local treatment to occasional spraying than to risk resultant exhaustion from more vigorous faucial cleansing.

The nose should be gently swabbed every two to four hours with warm saline or warm bicarbonate of soda solution. Forceful irrigation is unwise because of the risk of conveyance of infective material into the Eustachian tube. The nostrils and upper lip should be smeared with boric ointment or vaseline to prevent crusting and excoriation. Discharge from the mouth and nose must be carefully collected on rags or paper handkerchiefs and promptly burnt.

As a rule, with the administration of antitoxin, the temperature rapidly subsides and the remainder of the illness is uneventful. In children, pain in the tonsillar lymph glands is frequently complained of and a warm woollen scarf is comforting. Nephritis is now exceedingly unusual as a complication, and no special steps are required for its prevention. A daily inspection of the ear drums, especially in young children, facilitates the early diagnosis of otitis media and permits of treatment by paracentesis. It is well to remember that pain may not be complained of in this condition.

**Complications.**—Otitis media, nephritis, arthritis, adenitis and rhinitis are complications for the treatment of which the reader is referred to appropriate sections of this book.

**Toxic and Septic Attacks.**—Toxic scarlet fever, fortunately of rare occurrence in recent years, is characterized by an abrupt onset, a temperature from 105° to 107° F., persistent vomiting, profuse diarrhoea, delirium and extreme prostration; the rash is frequently inconspicuous. The onset of such symptoms in a child who has been in recent contact with scarlet fever is an urgent indication for immediate intravenous serum-glucose-saline administration. The treatment of the case is otherwise purely symptomatic, special measures being taken to combat cardio-vascular failure.

The septic type of scarlet fever which usually occurs in young children is a very serious disease. Antitoxin is less efficacious in such cases and systemic penicillin in a dose of 0.5 to 1.0 mega units daily should be begun at once. Particular emphasis is placed on the value of the open balcony. The grossly inflamed and painful throat and blocked nostrils may necessitate the rectal or intravenous administration of 5 per cent. glucose saline. Septic complications and broncho-pneumonia are of common occurrence, but the use of penicillin has greatly improved the prognosis of such cases.

**Convalescence.**—Providing the condition of the myocardium and the pulse is satisfactory, mild uncomplicated cases of scarlet fever may be allowed out of bed on the twelfth day of disease, and in suitable weather into the open air three days later. Patients suffering from severe or complicated attacks should be confined to bed for at least three weeks.

No definite isolation period can be advised which suits all cases. Provided there have been no septic complications, strict isolation may be relaxed after two weeks. During the subsequent week the patient should sleep by himself, have crockery, cutlery, handkerchiefs, towels, etc., reserved for his own use, and remain out of doors as much as possible. Where purulent discharges have occurred (*e.g.*, otitis media, sinusitis), these should be healed before freeing the patient. Fortunately, penicillin has greatly hastened the cure of such conditions.

During recent years the period of isolation in hospital has been reduced in suitable cases to 14-21 days without any ill results either to the patient or to his associates.

#### CARRIERS

The persistence of *S. pyogenes* in the fauces or nose cannot be regarded as a reliable index of infectivity, and the routine bacteriological examination of scarlatinal convalescents is to be deprecated. Nevertheless, a rich growth of this organism from either the throat or nose of certain patients, *e.g.*, dairy workers, nurses, medical men, school-teachers, may reasonably be regarded

as an indication for continued isolation until the carrier condition has ceased. Tonsillectomy will rid most faucial carriers of *S. pyogenes*. Antiseptic applications to the fauces and pharynx are ineffective. Sulphonamide snuff is worth a trial in persistent nasal carriers, and a powder containing sulphathiazole and penicillin (5,000 units-gm.) may be insufflated into nose and throat. A course of systemic penicillin in doses of 0.5 mega units per day for 5 days should also be tried.

## SMALLPOX

(*Variola*)

Of recent years two distinct varieties of smallpox have occurred in this country—variola major and variola minor. The latter appears to be endemic to certain parts of the country; the former is always the result of introduction from abroad. Clinically the two types are very alike, but whereas the fatality rate of major smallpox is around 15 per cent., that of minor smallpox rarely exceeds 0.2 per cent. The minor form is apparently due to a smallpox virus of low virulence and the disease breeds true. Vaccination is equally protective against both forms of the disease.

The virus of smallpox almost certainly enters the body via the respiratory tract. During the course of the infection, virus is discharged in the secretions of the mouth and nose and in the skin lesions. Bed linen is thus heavily infected and the air of the room becomes charged with the virus. Although infection is most often from case to case, papers, clothing, etc., may all act as a vehicle, for the virus appears capable of survival for long periods in the dry state. As a result, not only must the isolation of the case be complete but there must be the most stringent disinfection of all articles associated with the case prior to its transfer to hospital.

The incubation period is usually twelve days but may vary between ten and fourteen days.

Smallpox is a notifiable disease.

**Preventive Treatment.**—The control of smallpox is essentially a public health problem. The accurate diagnosis of the initial case or cases rests, however, with the practitioner, and herein lies a grave responsibility. Early diagnosis, followed by prompt isolation of the primary case, the immediate vaccination and continued supervision of all contacts, and thorough disinfection of the patient's house and its contents are the essentials of successful smallpox control. The practitioner should not hesitate, therefore, to obtain the opinion of an expert from the local Public Health Department on any case which he has the least reason to suspect might be smallpox. The initial case or cases in a smallpox epidemic are commonly misdiagnosed as chickenpox.

There can be no doubt as to the wisdom of promptly removing every case of variola major to hospital. Hospital isolation should be enforced during an epidemic of variola minor so long as accommodation is available. In the event of continued spread of the minor form, circumstances may justify or necessitate home treatment. These matters of policy are for the local Medical Officer of Health to decide.

After the removal of the patient to hospital, every member of the family and every known contact should be immediately vaccinated. Chil-

dren, unless recently successfully vaccinated, should be excluded from school for sixteen days from the date of last contact with the patient. Adult contacts who accept vaccination may continue their occupation, but should be examined morning and evening for a period of sixteen days. Adult contacts who do not accept vaccination should be strictly quarantined.

If a case of variola minor is treated at home, isolation of the patient should be strictly enforced and every member of the household vaccinated. Current disinfection must be conscientiously performed.

*Vaccination.*—In this highly effective method of prophylaxis against smallpox, introduced by Jenner in 1798, vaccinia, or cowpox, is inoculated into the human subject. Vaccinia is now regarded as a modified form of variola resulting from the passage of the smallpox virus through animals.

Although the vaccination of infants before the sixth month is still compulsory in this country, exemption can readily be obtained. Under the new Health Service Act compulsory vaccination in infancy will cease.

Primary vaccination should not be performed until the fourth month, and should be postponed if the child is debilitated, febrile or has recently been exposed to infectious disease. It should never be performed on an infant who is eczematous, for it is in such patients that generalized vaccinia is liable to occur. Exposure to smallpox, however, justifies immediate vaccination. Fresh glycerinated calf lymph, which is issued in sealed capillary tubes, should be employed. The lymph should be stored in a refrigerator. The contents of a tube once unsealed must not be kept for use on a future occasion. The lymph must be expelled from the tube by a rubber teat—such as that used on an infant's feeding-bottle; *the mouth must not be applied directly to the tube.*

The usual site for vaccination is over the insertion of the left deltoid muscle, but for æsthetic and other reasons the inner and posterior aspect of the arm or the outer aspect of the thigh or leg may be chosen. The skin should be cleansed with soap and warm water, wiped with industrial methylated spirit or ether and dried carefully. A drop of lymph is then expelled on to the cleansed area, and a single linear scratch  $\frac{1}{4}$  in. long made through the lymph in the long axis of the limb with a sterile needle. The scratch should be just deep enough to impart a pink colour to the exuded serum. The arm must not be covered until the lymph has dried. If the patient tends to scratch the vaccination site, a dressing of sterile gauze or lint may be bandaged on, but in most cases a dressing is unnecessary.

When the maximum degree of protection against smallpox is desirable (in smallpox contacts), then the number of insertions should be increased to four, situated at least 1 in. apart. Vaccination should be performed with the minimum of trauma to the tissues, and cross scarification avoided.

The duration of immunity to smallpox after primary vaccination is variable. Good "takes" to revaccination may be obtained even after the lapse of only one year. A distinction must be drawn between the results of primary vaccination and revaccination. In the former the resulting lesion does not reach a maximum until about the eighth day; in the latter the maximum evolution is reached on the third to fifth day.

Both of these reactions indicate that the individual was susceptible to smallpox and has now been rendered immune. There is a dangerous tendency in revaccination to regard slight local reactions which reach a maximum

in 24-48 hours as indices of immunity. Such an interpretation is without any foundation, for there may be three other explanations. First, the vaccination may have been unsatisfactorily performed; second, the lymph may have become degenerate; and third, the individual may be reacting merely to trauma or to the vaccine lymph. The last may be excluded fairly easily by carrying out a control vaccination with heated calf lymph. The others can only be excluded by performing the vaccination at least three times; at the last insertion an entirely different site should be chosen.

In the event of exposure to smallpox, vaccination should immediately be performed unless there is reliable evidence of successful primary vaccination within the previous three years or successful revaccination within the previous five years. The important words in the last sentence are "reliable" and "successful." In case of doubt, revaccinate. Owing to the risk of vaccinal encephalitis, slight as it may be, primary vaccination should not be performed in school-children or in adolescents unless they have been directly exposed to smallpox.

Successful vaccination (four insertions) within the first four days of the incubation period may prevent an attack of smallpox.

**Curative Treatment.**—There is no specific treatment for smallpox. The constitutional disturbance of the prodromal stage is treated on the lines already laid down (p. 2). The diet at this stage is limited to fluids, and water must be administered freely.

**Chemotherapy.**—The sulphonamides have not proved universally beneficial in the treatment of smallpox. No form of chemotherapy of course can affect the virus stage of the disease, but it was hoped that such treatment when given early might lessen the extent of the subsequent bacterial infection in the vesicles. The frequent failure of sulphonamides may be explained in two ways. First, the infecting organisms may be insensitive and staphylococci, which are often responsible, are at least relatively resistant to sulphonamides. Second, the sulphonamides are less effective in the presence of purulent accumulations and in the pustular stage of the rash conditions are certainly made unfavourable. If only sulphonamides are available, the drugs of choice are sulphadiazine or sulphathiazole and either should be given in full dosage. Administration should be begun as early in the illness as possible.

Fortunately, penicillin overrides the two difficulties which defeat the sulphonamides, for not only are they usually effective against staphylococci but they are also active in the presence of pus. It is desirable that the contents of the vesiculo-pustule should be submitted for bacteriological examination, however, for the type of organism present will decide the amount of penicillin required. For staphylococcus or *S. pyogenes*, 150,000 to 200,000 daily will suffice; but if the viridans type of streptococcus is involved a much higher dosage (500,000 units daily) is advisable. Here again treatment should be begun early, for the antibiotic may actually impede the development of the pustule and thereby greatly lessen the severity of the disease.

**General Management.**—During the papular and vesicular stages of the eruption the regular application of an antiseptic dusting powder (equal parts of boric acid, zinc oxide and starch) or boro-calamine lotion will help to allay the skin irritation. Along with the daily permanganate bath little else need be done in the treatment of variola minor. In this form of smallpox

the rash often aborts, secondary fever is usually absent and the prognosis is uniformly good.

Iced boric compresses applied to the face and distal parts of the limbs, and frequently changed, will be found comforting in the confluent eruption of major smallpox. Prolonged warm baths, spraying with a 1 : 40 solution of phenol or smearing the skin with 3 per cent. carbolic vaseline are alternative methods of treatment. In children the arms may require to be splinted or the hands bandaged to prevent scratching. Chloral and bromide given internally may give some relief and facilitate sleep; morphine aggravates skin irritation.

When the pocks begin to rupture, the patient, if not too ill, should be immersed three times daily for half an hour each time in a bath at 98° F.; either potassium permanganate may be added until the water has a claret tinge or a double handful of boric crystals.

The offensive smell associated with confluent cases of major smallpox can be masked to some extent by sprinkling eucalyptus oil on and around the bed.

The application of starch or linseed poultices spread thinly on lint will hasten the separation of the scabs, and subsequent tenderness of the skin can be alleviated by the application of sterile talcum powder or zinc oxide ointment.

The virus is susceptible to the action of potassium permanganate, so that painting the lesions with a 1-5 per cent. aqueous solution has a value not only against bacterial invaders but upon the virus. Contamination of the ward air is thus diminished.

Owing to the presence of the eruption on the mucous membranes, the eyes, mouth, throat, nose and larynx require careful treatment. The eyes should be bathed with warm boric lotion at four-hourly intervals, and 1 drop of 10 per cent. mild silver protein inserted morning and evening if conjunctivitis be severe. Vaseline applied to the margins prevents gumming together of the lids. The mouth and throat must be cleansed at regular intervals; either a 1 : 5,000 solution of permanganate of potash or peroxide of hydrogen diluted with two parts of water may be employed as a spray or mouth wash. Frequent inhalations of steam, impregnated with Friar's balsam or creosote, help to alleviate laryngeal and bronchial symptoms. Dysphagia may be lessened by sucking fragments of ice or by spraying the throat with a 4 per cent. solution of cocaine before each feed.

The fluid diet of the prodromal period requires to be supplemented by soft solids during the eruptive stage. Fresh fruit juice drinks sweetened with glucose must be administered freely throughout the illness.

**Complications.**—Boils and abscesses are of frequent occurrence, and should be treated on surgical principles. Severe laryngitis sometimes necessitates tracheotomy. Broncho-pneumonia is a common and frequently fatal complication. Keratitis and panophthalmitis are liable to occur in severe cases, particularly if the eyes have not been carefully treated from the first.

**Convalescence.**—The patient should be kept in bed until the eruption has crusted. In variola minor and in mild attacks of major smallpox convalescence is usually rapid and the patient fit for discharge from hospital or isolation as soon as he is free from infection. School or business activities may be resumed from two to four weeks after release from isolation.

After severe attacks, several months may elapse before the patient is fit to resume his normal activities.

Isolation must be continued until the last crust has separated from the skin. This period varies from three weeks in mild cases to three months or longer in severe attacks. Detachment of the crusts can be hastened by warm baths and the application of linseed or starch poultices, olive oil or vaseline. The thick skin of the palms and soles may be softened by frequent soaking in hot water, and the buried crusts picked out with a sterile pen-knife as recommended by Ker.

A thorough soap and water bath and shampoo precedes the transfer of the patient to a non-infected room in which he puts on clean clothes.

## TETANUS

The normal habitat of *Cl. tetani* is the intestinal tract of horses, cows and other herbivora. The bacilli are sometimes found in human faeces. Heavily manured soil is particularly liable to be contaminated with the highly resistant spores of the tetanus bacillus. Introduced through a punctured wound commonly made by a splinter or nail the bacilli, or spores, particularly in the presence of pyogenic infection, laceration of tissues and a foreign body, tend to multiply and produce the powerful toxin which acts on the nervous system.

Whilst the potential risk of tetanus following deep suppurating wounds is well recognized, the very real danger of infection following superficial septic abrasions in children or mild septic skin lesions in farm workers is not sufficiently appreciated. Imperfectly sterilized catgut has been responsible for the development of post-operative tetanus.

The length of the incubation period has a very important bearing on prognosis. When this period is less than seven days, recovery is unlikely. Should the spores lie latent in the tissues, the incubation period may be weeks or even months.

Early diagnosis is very important. Stiffness of the jaw, pain in the neck or back increased by manipulation and associated with the characteristic facial expression should lead to immediate specific treatment.

Tetanus is not a notifiable disease.

**Preventive Treatment.**—*Passive Immunization.*—If all accidental wounds were promptly and thoroughly cleansed and, in circumstances favourable to infection, tetanus antitoxin employed as a prophylactic, the disease would virtually disappear.

Where a wound is liable to be contaminated by dirt from manured soil, stables or farmyards, in lacerations by farm implements, in bites or wounds from horses, in gunshot wounds, etc., in addition to early and thorough cleansing of the injury an intramuscular injection of from 1,500 to 3,000 units of tetanus antitoxin should be given promptly. If the risk of tetanus appears to be great, then the prophylactic dose may be repeated eight days later, and invariably if the wound has to be re-opened.

*Active Immunization.*—Protection against tetanus, like diphtheria, may be obtained by the use of toxoids, *i.e.*, toxins which have been rendered safe by mixture with formalin but which still retain their antigenic power. Alum-precipitated toxoid and formol toxoid are the products most commonly used. Two injections of 1.0 c.c. are given with a minimal interval of four weeks between them. (When protection against several infectious diseases is required there is no reason why a combination of

prophylactics should not be given at the same time. For example, in the army the recommended procedure is as follows:—

Day 1—First dose of T.A.B. and first dose of tetanus toxoid.

Day 14—Second dose of T.A.B.: smallpox vaccination.

Day 28—Second dose of tetanus toxoid.)

As is the case with diphtheria, single injections of toxoid have little immunizing power. Indeed, in persons specially liable to exposure to tetanus, it is particularly desirable to give a third injection 9-12 months after the initial course. This produces a sharp and much more prolonged rise in antitoxin levels.

**Curative Treatment.**—The four essentials in the treatment of tetanus are: (1) the early administration of an adequate amount of antitoxic serum; (2) thorough cleansing of the wound; (3) sedatives to abolish spasm and rigidity; and (4) adequate intake of food.

**Antitoxic Serum.**—The early administration of an adequate dose of antitoxin is the first measure, and 200,000 units should be injected intravenously. It must be appreciated that the antitoxin will only neutralize free circulating toxin and can not unloose such toxin as is already fixed in the tissues. Antitoxin administered late in the disease cannot have any curative effect, for nervous tissue damage is already beyond the reach of serum. For this reason intrathecal injection of antitoxin is not now regarded as advisable.

**Cleansing of Wound.**—Owing to the possibility of increased toxic absorption it is a wise procedure to delay cleansing the wound until an hour or two after the intravenous administration of antitoxin.

Scabs and foreign bodies should be removed, penetrating wounds freely opened up and whitlows incised. After the evacuation of all septic material and the removal of lacerated tissue, the wound should be syringed with hydrogen peroxide and dressed with light porous gauze. Dressings should be changed every four hours. Free drainage is essential, the wound being kept open and allowed to granulate from the bottom.

General or regional anaesthesia may be required, but local anaesthesia or cauterization of the wound are inadvisable. Although penicillin may be of value to inhibit or to treat secondary infection, it has no effect upon the course of the tetanus infection.

**Control of Spasms.**—In mild cases without convulsions 30 gr. (1.8 gm.) of bromide of potassium administered every six hours is all that is required. If the spasms are severe, the period of onset less than four days or the patient becoming exhausted, then bromethol is the most efficacious drug to employ. From 0.07 to 0.1 gm. per kg. of body-weight should be administered by the rectum at intervals of six to eight hours. As the spasms diminish, the time interval between doses may gradually be increased. Apart from some respiratory difficulty and slight cyanosis, which is usually relieved by atropine hypodermically, and oxygen administration by the nasal catheter, no toxic effects have been observed.

Among the less reliable drugs that have been employed are chloral hydrate, from 15 to 30 gr. (0.9 to 1.8 gm.) every three hours; paraldehyde in doses of 2 to 6 drachms (7.2 to 21.6 c.c.) in 3 to 9 oz. of normal saline by the rectum; and morphine sulphate hypodermically up to 2 gr. (0.12 gm.) daily.

Inhalations of nitrous oxide and oxygen, chloroform or ether, may



be necessary in severe respiratory spasm until the bromethol effect is obtained.

The action of curare in interfering between muscle and nerve at its end-plate and thus inducing complete muscular relaxation suggests that this alkaloid may have a valuable place in the control of spasm in tetanus. There is as yet no standard procedure advised.

*General Management.*—The patient should lie on an air mattress or water-bed with the bedclothes supported by a cradle. Isolation is not essential. Trained day and night nurses are necessary. Noise must be excluded, the sickroom darkened and nursing duties performed quietly and preferably at times when the patient is deeply under sedatives.

A minimum daily food intake of 2,000 calories in an adult patient, whilst a highly important part of the treatment, is very difficult to attain. One of the main duties of the nurse is to feed the patient at hourly or even half-hourly intervals with milk, egg flip, thin gruels and glucose lemonade. To facilitate feeding, teeth may have to be extracted. Plain water or glucose saline should be given freely by the mouth or rectum. In severe cases feeding should be carried on through a nasal tube left in position or supplemented by the intravenous administration of 5 per cent. glucose saline by the drip method.

The bowels should be moved by enemata, and retention of urine watched for and relieved by catheterization.

## TYPHUS FEVER

Apart from a few sporadic cases occurring from time to time, particularly in Ireland and such ports as Glasgow and Liverpool, typhus fever, once so prevalent, has disappeared from this country. Exanthematic or epidemic typhus, the type of disease so prevalent in Europe, is caused by intracellular infection with *Rickettsia prowazeki* bodies, and is transmitted from man to man by lice. The *Rickettsia* bodies are present in the blood vessels of the skin, brain, kidneys, etc., and have also been found in the intestinal epithelium of lice taken from cases of exanthematic typhus. Infection is inoculated either through the bite of an infected louse or through the louse excreta being scratched into the skin. Of recent years a group of typhus-like diseases has been noted as occurring in various parts of the world—so-called endemic typhus. This group, in which ticks, mites and fleas are known vectors, include murine typhus, world-wide in distribution, *fièvre boutonneuse* in Mediterranean countries, *tsutsugamushi* disease (scrub typhus) in Malaya and Japan, and Rocky Mountain spotted fever.

The incubation period is usually from twelve to fourteen days, but may vary from five to twenty-one days. Under epidemic and famine conditions the period may be shortened to about eight days.

Typhus fever is a notifiable disease.

*Preventive Treatment.*—*Active Immunization.*—Several *Rickettsial* strains are responsible for the different forms of typhus infections and immunity seems to be specific. It is therefore necessary to know against which infection immunity is required. Against louse-borne or exanthematic typhus a variety of vaccines has been produced, some of which contain living virus whereas in others the virus has been killed. The former give rise to

a slight or latent infection and are not devoid of risk. Cox's vaccine, prepared from *Rickettsiæ* cultivated in the egg, is an example of a killed vaccine which was used widely during the recent war. Three doses, each of 1.0 c.c., are given at intervals of 7-10 days. If immunity is to remain satisfactory, boosting doses of 1.0 c.c. every 4-6 months are necessary. Mouse lung vaccine, which was developed particularly for protection against scrub typhus, has proved very satisfactory in creating a more prolonged immune response. The dose is three inoculations of 0.5 c.c., 1.0 c.c. and 1.5 c.c. subcutaneously at five-day intervals.

The proven efficacy of D.D.T. (see p. 278) has made it rather doubtful if active immunization of such short duration is worth achieving under field conditions. Although it is true that in the Naples epidemic of 1943-44 the medical personnel had received preventive inoculation at some time, their relative freedom from attack was probably more related to the liberal use of the powder. The ease of its application, allied with the duration of its effectiveness, make it an ideal measure for the protection of an exposed population.

*General Measures.*—The diagnosis of the sporadic case of typhus fever presents great difficulty. The practitioner should immediately enlist the help of the Public Health Service if faced with a suspicious case. Early and repeated Weil-Felix tests provide the most reliable generally available laboratory method of diagnosis. (It is worth noting that specific blood-agglutination against individual *Rickettsia*! suspensions now permits of a precise differentiation between the different forms of the disease.)

The essential factor in limiting the spread of typhus fever is the prompt delousing not only of patients and contacts, but of the community as a whole. If this is properly carried out complete protection is conferred. Disinfestation should therefore be regarded as the major preventive measure to which vaccination is subsidiary. Fortunately, the employment of the insecticide D.D.T. has already been shown to be highly effective as a practical measure in controlling typhus. It not only simplifies disinfestation but affords a high degree of protection to the personnel. Details of its application are given on p. 278.

Attendants should be immunized and preferably be under thirty years of age, since in the event of infection the prognosis is graver with increasing age. The use of D.D.T. as a dusting powder, and also impregnated into the clothing when laundered, provides an additional safeguard. Protective clothing is no longer essential.

All clothing and bedding must be removed for steam disinfection. Leather and rubber articles may be disinfected by immersing for ten minutes in a watery emulsion of 2 per cent. cresol with 5 per cent. soft soap.

Contacts are kept under daily observation for three weeks from the date of last exposure. Adults, following disinfestation, may be permitted to attend business, but children should be kept away from school throughout the quarantine period.

*Curative Treatment.*—*Serum Treatment.*—Claims have occasionally been made for convalescent human blood or serum and for immunized horse serum. The former has been given intravenously in a dose of 200 c.c., or intramuscularly in doses of 20 c.c. or more daily. The horse serum is given intramuscularly in daily doses of 20 c.c. for five days. The value of serum therapy has, however, not been widely confirmed.

*Chemotherapy.*—Rickettsiæ, like viruses, depend for their survival and multiplication in the human host upon their intracellular existence. Attempts at chemotherapy thus demand that the environment of the Rickettsiæ in the cell may be made inimical without at the same time affecting the viability of the cell parasitized.

It has been suggested that *p*-aminobenzoic acid fulfils this criterion, and favourable results have been reported from the use of 2.0 gm. two-hourly during the acute stage of the illness. These studies, however, require repetition under strictly controlled conditions. Two British sulphonamides which showed activity in the laboratory (*p*-sulphonamido-benzamidine hydrochloride and *p*-sulphonamido-benzamidoxime hydrochloride) have undergone clinical trial but no benefit from their administration could be shown. The usual sulphonamides are without effect. Penicillin, although ineffective against typhus itself, may have some beneficial action in combating secondary bacterial infection.

*General Management.*—Typhus fever is essentially a disease for hospital treatment, where, if possible, the patient should be nursed on the open balcony. Once the patient has been thoroughly freed from vermin there is apparently no risk of the spread of contagion to nurses or attendants.

Skilled nursing is essential. The diet and management of the case is on the same lines as advised for the treatment of a severe case of enteric fever.

Pyrexia, headache, insomnia and delirium call for frequent tepid sponging and the exhibition of hypnotics. The bladder should be percussed morning and evening, particularly in delirious patients, and retention of urine relieved by appropriate measures. The myocardium suffers severely in typhus fever, and every precaution should be taken to conserve the patient's strength. Azotæmia is a feature of the severe case and a persistently high blood urea is a bad prognostic sign. Daily intravenous injections of 5 per cent. glucose saline by the drip method may advantageously be employed in toxic cases.

*Complications.*—Whilst complications are uncommon, laryngitis, bronchitis, broncho-pneumonia and myocarditis may give rise to anxiety during the acute stage of the illness. Thrombosis in the veins or arteries, particularly in the lower limbs, is a feature of some epidemics.

*Convalescence.*—Strength is usually rapidly regained, but the reaction of the cardio-vascular system to increased effort must be carefully watched. The patient may be permitted to sit up in bed one week after the temperature has settled, and may get up a few days later. The appetite returns early and the diet may be rapidly increased. As the patient may be regarded as non-infective from the time of delousing, he may be permitted to leave hospital when fully recovered, but should not resume work for at least another four weeks.

## WHOOPIING-COUGH

(*Pertussis*)

A particularly dangerous disease in infancy, whooping-cough is one of the most important infections of early childhood. The disease is most infective during the catarrhal stage of the illness, the stage at which clinical diagnosis is very difficult. The causal organism is spread by direct contact,

droplet infection and perhaps by fomites. Abortive and unrecognized attacks are common, particularly in adults, and frequently prove an unsuspected source of contagion.

Early diagnosis is impossible on clinical grounds alone. Unfortunately, bacteriological diagnosis also presents difficulties although these are now less than they were. Pharyngeal swabs are to be preferred and may be taken either through the mouth or the nose. If a thin wire swab is obtainable the latter method is better. Isolation of the organism has been aided by the inclusion in the special medium of penicillin to which *H. pertussis* is resistant. Although most infections are probably due to *H. pertussis* there is evidence that some infections are due to an antigenically distinct strain called *H. parapertussis*. Other so-called aids to diagnosis are of less value. Thus complement-fixing antibodies only appear late in the illness. White cell counts (showing a marked lymphocyte preponderance) are useful in older children but of less value in infants.

The incubation period is from eight to fourteen days. The disease is not notifiable.

**Preventive Treatment.**—*Active Immunization.*—The use of vaccines for the prevention of pertussis has had a chequered career. Unfortunately, despite the long period of time in which they have been used, it is still only possible to give them qualified approval. The vaccine must in the first place be prepared from recently isolated strains in what is usually called the "Phase I" stage of growth. Vaccines made from such strains, containing 10,000 million organisms per c.c., can be obtained commercially. A prophylactic course requires a total dosage of 60,000 to 80,000 million organisms in three to five graded injections; but even such vaccines seem to vary in their antigenicity. The second difficulty may arise from the fact that an antigenically distinct organism, *H. parapertussis*, can cause whooping-cough; if immunity is specific to the type of organism injected (namely *H. pertussis*), failures might be due to infection with parapertussis strains. Finally, however, it must be admitted that, as with enteric vaccines, there is reason to believe that the stimulation of antibacterial antibodies presents greater difficulties than used to be appreciated.

Recently, whooping-cough vaccines have been prepared in combination with alum-precipitated diphtheria toxoid. It is undesirable that these reagents should be stored in contact with each other for long periods of time and it is therefore to be preferred that they should be kept in separate bottles and mixed in the syringe immediately prior to injection. If combined immunization is to be carried out, the first injection should be given at the age of six months, for, if the whooping-cough vaccine is to have any effect, the earlier in life it is given the better. The course consists of two injections of 1.0 c.c. with one month's interval between them.

*General Measures.*—The general public, and indeed the medical profession, require to be educated in the fact that pertussis is now the most serious infectious disease in infancy and early childhood. It is for this reason that it is particularly to be regretted that a reliable method of early diagnosis is not readily available, for the disease is most infectious during the early catarrhal stage when clinical diagnosis is difficult. Children suffering from "colds" and suspicious febrile upper respiratory catarrhs should be prevented from mixing with infants, especially when whooping-cough is prevalent in the district. When contact does occur the child should be rigor-

ously excluded from such places as nursery schools during a quarantine period of three weeks.

**Curative Treatment.**—*Specific Treatment.*—There is no serum or drug of proven value in the treatment of whooping-cough. Vaccine treatment is valueless. When broncho-pneumonia supervenes, sulphadiazine with penicillin must be given; but it has to be admitted that the results are often unsatisfactory.

*General Management.*—In the absence of specific treatment, reliance must be placed on measures designed to lessen the severity of the spasms and perhaps to prevent lung complications. Isolation of the child from all contact with others, especially adults, may have some effect in reducing exposure to secondary infection. If the condition of the child permits, strict confinement to bed is unnecessary and may be unwise. Movement assists in aeration of the lungs and it is undoubtedly true that the occurrence of collapse of the lungs is as much to be feared as broncho-pneumonia which it can so closely imitate. For the same reasons the sickroom should be well ventilated, and indeed, if the weather permits, a period out in the open daily is to be encouraged.

When the paroxysms are at their height it is essential for the child to be constantly under supervision so that it may be given assistance. With young babies, the old-fashioned method of throwing the child across the shoulder and vigorously patting the child's back has much to be said in its favour. Smacking the back during the paroxysm assists the expiratory phase of the cough and encourages deep inspiration.

The feeding of the infant and young child presents a serious problem. Advantage may be taken of giving the child its food after a paroxysm; or of lessening the interval between feeds to two hours and giving a reduced amount. During a moderate to severe attack it may be taken as invariable that the child will lose weight; and provided it is not excessive this should not give rise to undue anxiety. The fluid intake should be kept up by the use of orange and lemon drinks flavoured with glucose.

If the paroxysms become severe and frequent, the only method of relief is by sedation. For a child of one year one of the following may be tried—syrup of chloral hydrate, 10 m. (0.6 c.c.); syrup of codeine phosphate, 10 m. (0.6 c.c.); Dover's powder,  $\frac{1}{2}$  gr. (0.03 gm.); or phenobarbitone, gr.  $\frac{1}{8}$  (11 mg.). It must be admitted, however, that the results are not always satisfactory. Tincture of belladonna is worthy of trial in severe cases, but to be useful must be pushed until dryness of the mouth and dilation of the pupil herald undue toxicity. A preliminary dose of two minims (0.1 c.c.) three times per day may need to be pushed to 8 or 10 minims (0.5 or 0.6 c.c.) for satisfactory response.

It must be remembered that there is an undoubted nervous element in the paroxysm. Quietness in the sickroom is essential; any sudden disturbance of the child should be avoided.

**Complications.**—Collapse of lung, broncho-pneumonia, convulsions and gastro-enteritis are serious complications and a frequent cause of death in young children. Epistaxis and other hæmorrhages, whilst of comparatively common occurrence, are not of serious import. Well-marked cardiac dilatation may occur in severe cases. Otitis media is not uncommon.

For broncho-pneumonia, sulphadiazine and/or penicillin should be prescribed, though it should be remembered that many of the so-called broncho-

pneumonias are in reality atelectatic areas with secondary infection. Chemotherapy has not produced such clear-cut benefit in the broncho-pneumonia of whooping-cough as compared for example with measles.

When a child under two years of age is suffering from pertussis, the parent should be warned of the possibility of convulsions, and instructed to treat the complication by the prompt administration of a hot mustard bath with the application of cold water to the head.

A few whiffs of chloroform will usually terminate the convulsion. Morphine sulphate should then be administered hypodermically,  $\frac{1}{4}$  gr. (2.7 mg.) to a child one year old, and the sedative effect continued by rectal chloral, 5 gr. (0.3 gm.) in 1 oz. of warm milk repeated as necessary. Lumbar puncture is a useful procedure when the convulsions are repeated. Repeated convulsions, however, are a serious prognostic sign.

**Convalescence.**—Fresh air and plenty of good wholesome food are the essential requirements in convalescence. Care must be taken to protect the child against catarrhal infection or chill. If circumstances permit, a change of air to the seaside or to the country will prove very beneficial, particularly to cases with a persisting catarrhal condition of the lungs. Cod-liver oil and iron may be prescribed. The tendency of whooping-cough to rouse into activity a latent tuberculous process should be borne in mind.

The paroxysmal cough may persist for months in some cases, but the duration of the cough is no measure of the infectivity. The child gradually loses its infectiousness progressively from the time of appearance of the whoop; and as a rule may be regarded as non-infective four weeks after the appearance of that sign, despite its continuation.

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## SEPTICÆMIA

The varied clinical manifestations of this condition have their common basis in the signs and symptoms due to an infection of the blood. Transient invasion by pathological organisms, however, may often occur without any signs or symptoms of disease. Thus blood cultures taken immediately after extraction of a tooth usually show a growth of streptococci, while four hours later no growth can be obtained. On the other hand, streptococci may be obtained from focal disease in many situations in the body, such as a joint, a tonsil, a tooth abscess, without any infection of the blood.

Bacteræmia, of diagnostic and prognostic importance, frequently occurs in connection with focal lesions which are of such importance as to merit description under the heading of the local lesion. Examples are: typhoid fever, puerperal sepsis, pneumonia and subacute bacterial endocarditis. Although the passage of organisms into the blood in these and other conditions will often give rise to signs of septicæmia, such diseases are not dealt with in this chapter and the reader is referred to the appropriate section.

The causes underlying the production of the clinical state of septicæmia are not fully understood, but undoubtedly they include two main factors:—

1. The infection of fixed tissues by micro-organisms and the spread therefrom to the main blood stream by veins or lymphatics. This probably takes place by septic thrombo-phlebitis of minute vessels in the infected area.

2. The failure of the natural or acquired immunological properties of the blood, and of phagocytosis to overcome the entry of organisms into the blood stream.

Before the advent of penicillin and the sulphonamide series of drugs, no reliance could be placed on chemotherapy and, recognizing this, the older classifications of septicæmia laid stress upon the characteristic types of disease, the response of the patient, the attempts to build up acquired immunity and the general principles of therapy in fevers. Modern chemotherapy has completely altered this outlook, for favourable therapeutic results are for the most part very rapidly attained when the infecting organism is sensitive either to sulphonamides or to penicillin. Accordingly the approach of the doctor to treatment must also be radically changed and may suitably be expressed in these main rules:—

1. The early recognition of the septicæmic state.
2. The early determination of the nature of the infecting organism.
3. The determination of the sensitivity of the infecting organism to sulphonamide drugs or penicillin.
4. The rapid and adequate use of the appropriate drug.
5. The recognition of any focus of infection and its removal.

**The Recognition of the Septicæmic State.**—In many cases there is little room for doubt; some obvious localized lesion is present—a lobar pneumonia, or puerperal sepsis—and the primary disease itself calls for the use of sulphonamides or penicillin. It is quite wrong to wait until the organisms have multiplied in the blood stream and produced an easily recognizable state of septicæmia. As soon as the nature and susceptibility of the causal organism have been determined in the primary lesion, chemotherapy should be commenced. Such cases are not dealt with here, but are included under the heading of the primary disease.

In some cases the primary lesion is actually visible. It may be a surface collection of pus such as a boil or a carbuncle; it may be an infected wound. Sometimes septicæmia follows the formation of an abscess which may occur in the site of the original lesion, such as lung abscess following pneumonia. Sometimes the abscess occurs at a different site in the body, such as cerebral abscess in a case of bronchiectasis. In many instances septicæmia is described as cryptogenic in origin, for the primary lesion cannot be determined. Sometimes careful search may detect a focus in the teeth, tonsils or nasopharynx. Often, however, the condition results from a scratch or a trifling wound which has quickly healed and the subsequent incubation period may be of many days or even weeks.

The doctor must therefore at all times be on the watch for the earliest signs of blood infection. The earlier suitable treatment can be started, the greater will be the percentage of rapid cures. Unexplained variations in temperature and pulse rate, unexplained sweating, an increase in malaise, in pallor, a rise in the number of leucocytes or a rigor should at once arouse suspicion and a thorough search should be made for the causal organism in the blood.

**The Nature of the Infecting Organism.**—Sometimes the nature of the primary lesion gives an obvious clue to the nature of the infection. Subacute bacterial endocarditis is due, as a rule, to the *streptococcus viridans*. Nevertheless there are other organisms which may occasionally cause this disease. Similarly, septicæmia may appear to be caused by an obvious gonorrhœal

urethritis, yet the organism in the blood stream may be one from a secondary infection of the urinary tract. Thus even the apparently obvious must not be taken for granted.

Blood must be obtained by venipuncture, p. 927, but further precautions, not outlined there, are necessary in order that contamination by organisms may be avoided. The writer employs the following technique: a Clinic Record fitting needle is fixed on a 10 c.c. Record syringe. The size of the needle varies from No. iv to No. 14 according to the size of the available veins. The needle and syringe are sterilized together and the junction of the needle and syringe is never again touched. This is a common site of contamination, and to avoid the need for adjusting the needle it should, at the beginning, be pressed firmly home on the nozzle of the syringe. A vein in the anticubital fossa is selected if possible; the arm is extended and a sphygmomanometer cuff is placed well above the elbow joint. Pressure is maintained at about 80 mm. of mercury. A clean towel is laid over the vein of choice and the vein is lightly slapped several times with the fingers, but not the palm of the hand. Sterilization of the area is accomplished by pouring a little absolute alcohol (nowadays, surgical spirit) on the site of puncture. No rubbing is permitted. After 30-60 seconds the vein may be punctured. If any form of sterilization of the skin which entails rubbing or scrubbing is employed, it has been found that a proportion of cultures will show a contaminant growth, such as *staphylococcus albus*. Ten c.c. of blood are slowly drawn into the syringe and the needle is then withdrawn from the vein. The point of the needle is dipped for a moment into surgical spirit and allowed to dry for a second or two. Three to five c.c. of blood are then injected through the rubber-capped top of bottles of media obtained from the bacteriologist. The top should be sterilized in the same way as the skin, by pouring on a little alcohol or surgical spirit. At least two bottles should be inoculated; one containing glucose broth for general purposes, and one with added bile salts for coli-typhoid organisms. Often, special media for the culture of anærobic strains are desirable. The inoculated bottles should be sent as soon as practicable to the bacteriologist. The postage of specimens is considered to lead to too long a delay with too high a percentage of negative results. Unused bottles of broth will remain sterile for an indefinite period, and may be stored. Every practitioner should have at least one set in his possession for immediate use so that no time need be wasted.

Blood should be withdrawn during a rigor if possible, or during the gravescent stage of fever. A single negative result should not be considered sufficient. If there is real suspicion of septicæmia blood should be withdrawn on three successive days without waiting for the result of the first specimen, and, if septicæmia is still considered possible, three specimens on one day, morning, middle of day and evening, should be taken. Even then the possible intermittent passage of organisms into the blood stream from some hidden focus must be kept in mind and the whole procedure repeated whenever it seems desirable.

If a positive culture is obtained and treatment started, the need for further cultures must be remembered. This is partly to determine the progress of the disease by ascertaining the quantity of the infecting organisms, partly to determine the continuing susceptibility to sulphonamide or penicillin, and partly to determine cure. Cultures should also be obtained



at once if any suggestion of relapse is entertained. The writer has seen a change of organism in culture on more than one occasion when there has been a focal infection present, and this change in infection may require an immediate change in treatment.

Finally, it should be recognized that sulphonamides and penicillin may very quickly sterilize the circulating blood, and even when, on clinical grounds, the immediate use of these drugs is indicated, the first culture should, if at all possible, be made before any drug is administered.

Cultures should also be made from any open infected lesion, though blood culture must never be omitted. It frequently happens that a mixed growth is obtained from the wound, and this cannot determine accurately the nature of the infection in the blood stream.

**Sensitivity to Sulphonamides and Penicillin.**—This is the duty of the bacteriologist. It need only be said in respect of his part, that he usually employs a standard strain of *staphylococcus aureus* called "Oxford" strain. He must also determine the sensitivity in a quantitative manner as compared with his standard strain. This further information is of no immediate practical value to the clinician, but when repeated cultures are made it shows whether or not the infecting organism is becoming resistant to the drug employed. This may call for a change from penicillin to sulphonamide; or from one sulphonamide to another member of the group, or from sulphonamide to penicillin.

The practitioner must know what organisms are susceptible, and this information is given on pp. 74 and 87. The determination of sensitivity lies at the very root of the successful use of sulphonamides and penicillin. If the organism does not belong to a sensitive group or if resistance to these drugs is acquired by the organism, then their employment is a pure waste of time and drug. Resistance is, however, very rare at the outset in the sensitive groups.

**The Use of the Appropriate Drug.**—As a preliminary to this short discussion the reader should study the sections on sulphonamides (p. 71) and penicillin (p. 86). Particular attention should be directed to methods of administration, noting especially the conditions under which penicillin rapidly deteriorates to become inert.

The sulphonamide drugs have been in use in this country since 1936 and are therefore widely known to the medical profession as a whole. Supplies of penicillin are now adequate for all purposes but may only be supplied after prescription by a medical man. The writer believes at the present time that in all cases of septicæmia penicillin should be the first drug of choice provided that the infecting organism has been shown to be penicillin sensitive. Penicillin is less toxic than the sulphonamides and even more rapid and certain in sterilizing the blood stream. If the case is not to be treated in hospital, penicillin is best given by intramuscular injection every three hours. The total dosage in twenty-four hours should be 200,000 units—that is to say, 25,000 units every three hours.

Therapeutic results in infection with sensitive organisms are dramatic. The signs and symptoms of the septicæmic state commence to disappear within twenty-four hours. The temperature and pulse rate return to normal by rapid lysis, sometimes even by crisis. The blood culture should be sterile within a week in all cryptogenic cases, and failure to secure such a result should lead to very careful clinical examination for any focus of

sepsis. This re-infection of the blood stream has often been seen during the management of cases of subacute bacterial endocarditis, and it is known that the organisms in the deeper portions of the vegetations on the cardiac valves are not readily accessible to penicillin circulating in the blood stream. Re-infection may also take place from abscess formation, small or large, superficial or deep.

As a general rule penicillin therapy may be stopped when the blood culture is sterile—this will entail continuing the use of the drug during the twenty-four or forty-eight hours needed to obtain culture results. If repeated cultures are not possible, treatment may be stopped after the temperature has been normal for thirty-six to forty-eight hours, though much more prolonged dosage is necessary in the case of bacterial endocarditis (see p. 610). There is nothing to be gained by gradually reducing the dose of penicillin, which, like sulphonamides, should be given in full dosage or not at all.

If the infecting organism is not sensitive to penicillin but is sensitive to sulphonamide therapy, the latter series of drugs is used. The indications for the drug of choice are set out on p. 73 and the dosage on p. 74. Parenteral administration (p. 76) should always be employed if the infection is fulminating in type or if the patient is unconscious. The considerations which govern the use of penicillin are the same for the employment of the sulphonamides.

**The Focus of Infection and its Removal.**—At the onset of septicæmia there may be an open wound which is the cause of the infection. In such cases a powder made up of 2,000 units of the calcium salt of penicillin to one gram of sulphathiazole should be used (p. 92). This procedure is of value in the prevention of septicæmia.

Abscesses of the subcutaneous tissues should not be incised but should be dealt with by aspiration and replacement of penicillin and saline in the cavity (p. 92). Abscesses in deeper structures of the body, or in the serous cavities, are handled on similar lines (p. 92). It must be realized that the oral administration of sulphonamides or the intramuscular administration of penicillin is relatively useless in dealing with collections of pus, possibly owing to local thrombotic changes in the blood vessels in the vicinity of the abscess.

In the majority of cases the specific measures outlined are sufficient to attain a cure. Occasionally, however, resistance to the drugs develops in a partial degree and the usual dosage fails to sterilize the blood. In these cases the drug may be changed or, rarely, the dosage greatly increased. Sometimes, however, it is necessary to fall back on the older methods of treatment. In such cases blood transfusion is advised.

The original method employed was the administration of whole blood. Many attempts have been made to increase the antibacterial efficacy of the blood, but these are complicated and of uncertain value. The practitioner is advised to rely upon simple transfusion. Large quantities of blood are seldom required, and 200 to 300 c.c. of whole blood will usually suffice. As many cases of septicæmia respond quickly to the administration of penicillin or sulphonamides, blood transfusion is not usually indicated during the first few days of treatment, but if the response is not satisfactory or is delayed unduly, blood transfusion should be given. Transfusions should be repeated from time to time if even transient benefit is seen. In the early stages a blood transfusion is given to administer normal serum and

leucocytes; only in the later stages, when anæmia becomes marked, is it intended to supply hæmoglobin and erythrocytes. Blood banks have been established in many parts of the country, and their recent development includes the provision of plasma without any of the cellular elements. Plasma is of value in the treatment of septicæmia if whole blood is not easily obtained and no high degree of anæmia has appeared.

Sera and vaccines are of practically no value. Many antiseptics have been tried in the past but have accomplished very little.

**General Measures.**—Diet should be light but ample. Fluid intake should be high and amount to at least 3,000 c.c. in the twenty-four hours for an adult. Glucose is valuable and the administration of 4 oz. a day is of benefit to the heart muscle. Additional quantities of vitamin A (cod-liver oil), vitamin B (marmite or yeast) and vitamin C (orange or lemon juice) should be given. Eggs, in moderate quantity, milk, soups and soft foods should make up a diet with a high calorific value giving a low residue, and should be administered in frequent small feeds. If the disease be chronic, little restriction should be placed on the patient's natural desires. Alcohol, approved by some, disapproved by others, is probably only of benefit in an emergency. Its food value is easily supplanted by glucose, and its stimulant effect by aromatic spirit of ammonia. Champagne, iced and in small quantity, is probably the best variety to employ.

Drugs, other than specifics, should be kept to a minimum. Acute circulatory failure may develop. Its treatment is discussed on p. 678. If pain be present,  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. (11 to 16 mg.) of morphine may be given by injection. For sleeplessness any favourite hypnotic may be employed; there are no special indications. An enema or a glycerin suppository is preferable to laxatives by mouth, other than paraffin, but here, too, any routine laxative treatment may be given, avoiding any preparation containing sulphur.

If anæmia develops, 30 gr. (1.8 gm.) of iron and ammonium citrate should be given three times a day.

The practitioner must never regard the prognosis as hopeless in a case of septicæmia. If a septic focus can be adequately drained, if penicillin or sulphonamides can inhibit bacterial growth in the body and if immunity can be stimulated, the most dramatic results can be achieved. At present the therapeutic measures in order of importance are penicillin, the sulphonamide series of drugs and blood transfusion. The actual management of any given case of septicæmia calls for the highest grade of clinical observation and judgment, and the successful outcome not infrequently is a measure of the care of the doctor, alike in the employment of the major methods of therapy and in the handling of the minor symptoms which may arise from day to day in the course of the illness.

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## SERUM REACTIONS

The introduction of the new refined serums has rendered acute anaphylactic reactions much less common than used to be the case, and the fear of causing anaphylaxis should not make the practitioner withhold serum if the indications for its administration are present. For example, 4,000 units of diphtheria antitoxin are contained in a bulk of approxi-

mately 1 c.c. and 3,000 units of scarlet fever antitoxin in approximately 1.9 c.c. With such refined serums, which are given intramuscularly, the occurrence of late serum sickness is limited to not more than 5 per cent. of the cases to which they are administered. Nevertheless, in sensitive people, serum reactions do occur even with refined serums, and when large quantities of serum are given intravenously the danger of anaphylaxis is very real. The reactions which occur may be divided into two main groups:—

1. Due to acquired or inborn sensitivity of the patient to foreign protein.
2. Due to causes other than allergy.

**Reactions due to Serum Sensitivity.**—The reactions may occur within seconds or minutes of the intravenous injection of serum or may not appear for one or two hours. When they occur in close proximity to the time of injection they are called anaphylactic reactions, but when they occur some days later (usually about the seventh day) they are called serum sickness.

Anaphylactic reactions may usually be recognized as belonging to one of two types. In some cases the principal feature is the appearance of a severe asthmatic attack due to bronchial spasm, whereas, in others, gastrointestinal symptoms such as nausea, vomiting and defæcation may appear. These latter symptoms are believed to be associated with spasm of the capillaries of the liver.

**Tests for Sensitivity.**—Before serum is administered parenterally, it is advisable to test for sensitivity. This is done by making certain inquiries and carrying out certain tests. A careful history should be obtained from the patient in regard to (1) previous attacks of asthma, hay fever, eczema, urticaria, etc., and, in particular, if such symptoms were re'lated in any way to sensitivity to horse serum, horse hair, horse dander and rabbit fur, since the horse and the rabbit are the two animals commonly used for the production of immune serum; (2) previous injections of, and reactions to, immune serum, *e.g.*, diphtheria or tetanus antitoxic serum.

If a negative answer is obtained to these two inquiries it is usually unnecessary to undertake the special tests for sensitivity described below, particularly if the serum is going to be given by the subcutaneous or intramuscular route. If, however, a positive answer is obtained to one or other of the inquiries a test for sensitivity must be carried out.

There are two tests commonly employed in testing for sensitivity.

1. *The Intradermal Test.*—0.2 c.c. of normal saline is injected into the skin of the volar surface of the forearm. If the control injection of normal saline is done first, the same syringe and needle can be used for introducing intradermally 0.2 c.c. of a 1 in 100 dilution of normal horse serum, 2 in. distant from the control. A positive reaction is recognized by the appearance in from five to twenty minutes of a wheal of at least 10 mm. in diameter surrounded by a zone of redness. This test is more difficult to interpret than the ophthalmic test, and less reliance can be placed upon it unless the wheal and flare are well marked, and extension of the wheal in the form of pseudopodia is present.

2. *Ophthalmic Test.*—Since rabbit serum produces a positive intradermal reaction in most normal individuals, the ophthalmic test must be used when testing for sensitivity. One drop of 1 in 10 dilution of immune horse serum or 1 in 100 of immune rabbit serum is instilled into one eye. The other eye acts as a control. A positive reaction consists of itching, lacrymation and injection of the conjunctiva within a few minutes, in which case the eye

should be immediately flooded with normal saline to remove the serum followed by the instillation of a 1 in 4,000 solution of adrenaline. When lacrymation occurs excessively, as is common when the test is carried out in children, the test serum may be so diluted that a false negative result is obtained.

**The Value of Tests for Sensitivity.**—Due caution is required in the assessment of the value of the tests for sensitivity. We have had patients with negative tests for sensitivity who have had reactions and others who have had no reactions despite the presence of positive tests. In general, however, it may be said that a history of previous allergic manifestations and sensitivity tests are both of value, because the liability to, and the intensity of, reactions is usually greater in those who give positive results than in those who do not. Thus, Bullowa had 36 patients suffering from pneumonia with anaphylactic reactions among 79 showing skin tests, as against 58 with reactions among 197 with negative skin tests. On the other hand, the same worker states that among 3,250 patients treated with serum 8 deaths (0·2 per cent.) occurred in such close proximity to the intravenous injection of serum as to suggest that they were anaphylactic in origin. In all 8 cases, both inquiry for previous allergic manifestations and tests for sensitivity were negative. It is clear, therefore, that even in the presence of a negative history and tests, the greatest care should be taken to administer immune serum extremely slowly as described below, and to have in readiness a syringe filled with potent adrenaline. Adrenaline should be contained in tightly stoppered bottles or glass ampoules, as it is rapidly oxidized if exposed to air.

Patients for whom serum therapy is contemplated may be classified into three groups :—

1. Patients in whom a negative history is obtained for asthma, hay fever, etc., and who have not received a previous injection of immune serum. Such patients can receive, without further investigation, the requisite immune serum, with reasonable safety, particularly if the serum is given slowly and by the intramuscular route.

2. Patients with hay fever or with asthma not related to horse emanations, or who have had a previous injection of horse serum, if the tests for sensitivity to horse serum are negative, may be given serum provided the risks involved are recognized and the injection is given extremely slowly and discontinued at the first sign of anaphylaxis. The risk of this may be considerably minimized by the previous administration of one of the anti-histamine drugs (see p. 96). It is recommended that 150 mg. of Benadryl or 300 mg. of Anthisan should be given orally exactly one hour before the serum is administered.

3. Patients from whom a clear history of asthma caused by emanations from horses or in whom the eye test is positive or the intradermal test strongly positive should not be given serum, especially by the intravenous route. In general this rule should not be departed from unless a careful consideration of the factors influencing prognosis suggests that the risks of anaphylaxis are more than counterbalanced by the benefits which may be expected from serum therapy. For instance, the administration of serum to sensitive patients suffering from pneumonia or hæmolytic streptococcal infections is no longer justifiable since the introduction of sulphonamide drugs and penicillin. On the other hand, in such dangerous diseases as diphtheria

or tetanus, in which serum therapy still constitutes the only form of specific curative treatment, it may be justifiable to take the risk of giving serum parenterally to sensitive patients, especially now that it is known that antihistamine drugs give some measure of protection against anaphylaxis. In such a case desensitization must be attempted under the protective "cover" of an antihistamine, which must not, however, engender a false sense of security so as to permit of any relaxation in scrupulous attention to the details outlined below:—

100 mg. of Benadryl or 300 mg. of Anthisan are given orally. Exactly one hour later the administration of small amounts of serum is started. The initial dose should be 0.25 c.c. subcutaneously, followed by 0.5 c.c. and 1 c.c. at hourly intervals. If no reaction occurs within one hour the remainder of the therapeutic dose may be given very slowly. Should a reaction occur, the administration must be stopped and 7 to 10 minims (0.4 to 0.6 c.c.) of a 1 in 1,000 solution of adrenaline must be given. By this means it may be possible, although at considerable risk, to continue the serum treatment some minutes later during the refractory period (anti-anaphylaxis). In general, severe reactions, whether allergic or thermal, indicate the discontinuance of the administration of serum.

**Treatment of Anaphylaxis and Serum Sickness.**—*Anaphylaxis.*—At the first sign of anaphylaxis 0.5 c.c. of a 1 in 1,000 solution of adrenaline hydrochloride should be given intramuscularly. Massage at the site of injection increases the rate of absorption. The injection should be repeated in a few minutes if relief is not obtained. The shock in severe cases demands immediate treatment by lowering the head, administering stimulants, e.g., sp. ammon. aromat. (1 drachm in water), brandy or whisky (4 drachms in water) or coramine (1 to 2 c.c. intramuscularly), surrounding the patient with hot bottles or the electric cage and administering oxygen through a nasal catheter. Artificial respiration may have to be started. If the blood pressure has fallen greatly, a transfusion of 500 to 1,000 c.c. of plasma or blood may be given.

*Serum Sickness.*—Serum sickness is recognized by one or more of the following manifestations: malaise, rise in temperature, pains in the muscles and joints, urticaria and eosinophilia. It may commence at any time between the first and the twelfth day after the injection of serum. The commonest day for the occurrence of arthralgia is the seventh. The symptoms may be mild or severe.

The administration of antihistamine drugs (see p. 96) is the treatment of choice in the control of serum sickness. They are most effective in abolishing the urticaria and irritation of the skin, but have less influence upon the pyrexia and arthralgia, for which latter antipyretics and analgesics, such as a powder containing 10 gr. (0.6 gm.) of acetyl-salicylic acid, 5 gr. (0.3 gm.) of phenacetin and  $\frac{1}{4}$  gr. (16 mg.) of codeine, can be given every four hours until the pain is relieved. Putting the joints at rest by splints is also of value when pain and swelling are marked. Four doses of 100 mg. of Benadryl or 200 mg. of Anthisan should be given orally during the waking hours at well-spaced intervals, and this treatment should be continued till all signs of serum sickness have disappeared, which may take about a week.

**Reactions not due to Allergy.**—*Vasovagal Attacks.*—Very rarely the patient may collapse when the needle is introduced into the skin. The patient is suffering from a "faint" or vasovagal attack, as recognized by the

pallor of the face, bradycardia, weak pulse and low blood pressure. Treatment consists of lowering the patient's head to improve the circulation to the medulla and the administration of diffusible stimulants. Occasionally, it may be necessary to inject adrenaline and to carry out the other measures described for the treatment of shock.

*Thermal Reactions.*—These reactions occur within thirty to ninety minutes of the injection of serum, and can be recognized by the presence of chill (rigor or shivering), rise in the temperature, malaise and sometimes nausea and vomiting. The rigor is followed by sweating. Thermal reactions occur in about 20 per cent. of patients receiving serum.

The chances of a thermal reaction are greatly reduced (1) if scrupulous attention is paid to the preparation of rubber tubing, syringes, needles, etc., used for the injection of the serum, and if refined and concentrated serum is employed which past experience has shown to be free from thermogenic substances; (2) if serum is administered very slowly.

During the stage of chill the patient should be kept warm with hot blankets and hot bottles, hot fluids should be given along with 15 gr. (0.9 gm.) of aspirin, repeated, if necessary, in one hour. If the temperature rises unduly high, the patient should be cooled down by placing on his forehead, wrists and ankles towels wrung out of iced water. Ephedrine is of no value. According to Bullowa, adrenaline increases and prolongs the rigor and hence is contraindicated, while amyl nitrite shortens the reaction.

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# THE CLINICAL USE OF THE SULPHONAMIDE DRUGS

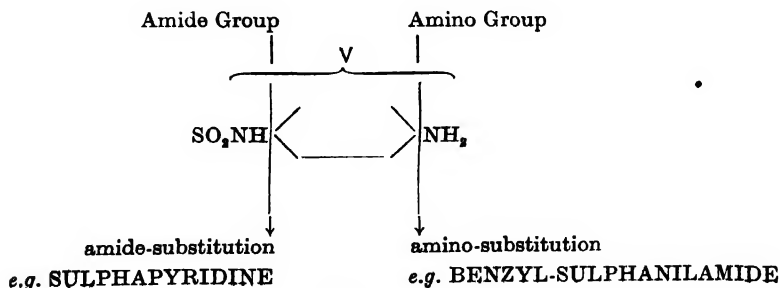
**N**O other single group of drugs, with the possible exception of penicillin, has such a wide application in clinical medicine as have the sulphonamides. Accordingly a separate chapter dealing with the group as a whole is desirable. The wise use of these drugs in any disease demands a proper appreciation of certain principles which are generally applicable; for, although a great deal remains to be discovered not only about their precise mode of action but even of their relative merits, it is already possible to say much of a definite nature. It must be understood at the outset that many of our conclusions are of a tentative character; but there is no harm in stating our present knowledge dogmatically, provided that the practitioner realizes that the primary object has been to give advice of an essentially practical nature.

## THE DRUGS

Prontosil Red (sulphamido-chrysoidin), the original dye introduced by Domagk in 1935, is now rarely used. (The word "Prontosil" has unfortunately become set in the minds of many doctors, and it is well, at the outset, to be clear that this proprietary name can be properly applied only to the one drug, sulphamido-chrysoidin.) It was an early observation that after absorption, sulphamido-chrysoidin was broken down in the body and a simple chemical compound, *p*-amino-benzene-sulphonamide (sulphanilamide), produced. Clinical experiments with this new drug in streptococcal infections soon showed that it achieved results differing little from those of the original dye, which it rapidly replaced in therapeutics. From it, two main groups of substances have been produced (see diagram).

**Group (a) : Amino-substitution Compounds.**—A considerable number of substances have been formed by substitution of the amino-grouping (*e.g.*

## SULPHANILAMIDE





Proseptasine (benzene-sulphonamide), Sulphonamide E.O.S., and Rubiazol). These drugs are all alike in this respect, that in the body, their fate is to be broken down to produce sulphanilamide. They in no way widen its range of clinical efficacy; they are useful only in those infections which are susceptible to sulphanilamide; in other words, they act as mere vehicles for their parent. It has been suggested that they are less toxic than sulphanilamide: but this is probably dependent upon the amount of sulphanilamide to which they give rise. For these reasons we advise that sulphanilamide should be the only drug of this series to be retained.

Unfortunately, manufacturers have placed this simple radical on the market under a wide variety of names. These are unnecessary, and often misleading; the drug should be prescribed as "Sulphanilamide." This criticism applies to all of the sulphanilyl derivatives; the practitioner should use, and name, the drugs as they are described in this chapter.

**Group (b): Amide-substitution Compounds.**—When substitution is made at the amide position a quite different series of compounds can be produced. The first of these newer substances was sulphapyridine, but since its introduction many others have been synthesized, the best known of which are sulphathiazole, sulphadiazine, sulphamezathine, sulphamerazine, sulphaguanidine and sulphasuxidine. The great importance which attaches to all the members of this group is, in the first place, that unlike the substances mentioned in group (a) their action is not dependent upon preliminary breakdown to sulphanilamide in the host. More important, however, from a practical point of view was the discovery that they exerted an action upon organisms which were beyond the range of sulphanilamide. The introduction of the amide-substitution compounds has had two main objectives: first, to widen still further the range of activity; and second, to lessen the unpleasant side effects which accompanied treatment with sulphapyridine.

These two main groups of drugs do not exhaust the list of chemotherapeutic substances which have been discovered as a result of the introduction of sulphamido-chrysoidin. A rather different series of compounds (the parent of which is diamino-diphenyl-sulphone) has been found to exert a similar action; with many of them their increased toxicity in man more than offsets their increased activity.

### ABSORPTION, DISTRIBUTION AND EXCRETION

Although there is considerable difference among the various drugs in regard to their solubility (in most cases it is low) they are all, with the exception of sulphaguanidine and sulphasuxidine, well absorbed from the alimentary tract, in the main from the small intestine. After oral administration of a single dose of sulphonamide a maximal concentration in the blood is reached in about three to four hours: thereafter the concentration slowly falls until at the end of twenty-four hours it has disappeared from the blood. On the basis of this experimental finding, administration of the drugs at four-hourly intervals is advised, in order to maintain a steady concentration of drug in the blood stream. Further, especially with the amide-substitution compounds where absorption is slightly slower, it is wise to

initiate treatment with a "loading dose" which is double that of the four-hourly one. This is particularly true in severe infections where it is desirable to secure an adequate concentration in the blood as rapidly as possible.

After absorption, the drugs pass into practically all tissues and body fluids, attaining there concentrations slightly less as a general rule than those which are obtained in the blood stream. In the liver, part of the drug is conjugated into an acetylated derivative. The amount of drug which is acetylated varies with the different drugs and with the duration of their administration. Two important aspects of this chemical change may be stressed. Firstly, the acetylated drugs are therapeutically inactive; secondly, they are all even less soluble than the parent drug.

The low solubility of the sulphonamides has particular importance in regard to their excretion, which is very largely by way of the kidneys. After filtration through the glomeruli, the filtrate is concentrated in the tubules so that the final level of the drug in the renal pelvis may be twenty to thirty times that in the blood stream. Such a change in the concentration of drugs which are in themselves of low solubility constitutes a possible danger. This danger is increased when we realize that the drugs appear in the urine in both the free and the acetylated form. If the urinary flow is diminished for any reason, crystals may form in, and block, the renal tubules—a very serious complication. It is, therefore, essential to ensure an adequate urinary output. This is of particular importance in febrile states and in hot climates where, despite a high fluid intake, excessive perspiration may occasion a low urinary excretion.

Two drugs (sulphaguanidine and sulphasuxidine) have been especially prepared for the treatment of infections of the alimentary tract because of their slow rate of absorption. Thus, even with a high oral dosage, the concentration obtained in the blood stream remains low, while the concentration in the bowel is high.

### CHOICE OF DRUG

Since the action of the drugs is of an antibacterial nature, and since it is very likely that the activity of the different drugs against different bacterial families varies, it follows that a knowledge of the bacteriological etiology of the disease to be treated is essential. Two general diagnostic implications may here be stated. Although, on the one hand, certain clinical diagnoses, for example erysipelas, identify a specific micro-organism, there are, on the other hand, many occasions when the clinical diagnosis must necessarily await the results of bacteriological examination before the identity of the infecting micro-organism can be established. The latter occasion is the more common one in clinical practice, and such circumstances demand that the drug to be used must be that with the widest known range of activity. The choice will rest between sulphathiazole, sulphamezathine or sulphadiazine, and one of these drugs should be given at once. When bacteriological proof of the etiological agent has been obtained it is possible to recommend a particular sulphonamide, and for these our choice is shown in the accompanying table:—

	1st Choice	2nd Choice
Streptococcal . .	Sulphanilamide	Sulphathiazole
Pneumococcal . .	{ Sulphathiazole Sulphamezathine	{ Sulphadiazine
Meningococcal . .	Sulphathiazole	Sulphanilamide
Gonococcal . .	Sulphathiazole	Sulphadiazine
Staphylococcal . .	{ Sulphathiazole Sulphadiazine	—
Dysenteric . .	{ Sulphaguanidine Sulphasuxidine	{ Sulphadiazine
Coliform. . .	Sulphanilamide	Sulphathiazole
Others ( <i>e.g.</i> <i>Cl. welchii</i> )	{ Sulphadiazine Sulphathiazole	{ Sulphamezathine

The frequent occurrence of severe vomiting when sulphapyridine is administered has caused us to regard it as a drug which should not normally be used, since it possesses no special character as a sulphonamide which will not be found in sulphathiazole, sulphamezathine or sulphadiazine.

We have been unable to convince ourselves that there is much to choose between sulphathiazole, sulphadiazine, sulphamerazine or sulphamezathine, whether regarded from the point of view of therapeutic activity or freedom from toxic effects. Apart from the slight difference in dosage schedule for sulphamerazine (see p. 75), each of the others may be prescribed in similar dosage and for similar conditions. It is very desirable that the practitioner should choose one of the compounds and use it for some time so as to acquire a thorough experience of its action and side effects.

## METHODS OF ADMINISTRATION AND DOSAGE

### THERAPEUTIC

**Oral Administration.**—It has already been explained that the rate of absorption from the alimentary canal is rapid. Therefore, in most infections, effective treatment may be ensured by oral administration alone.

The drugs are usually supplied in tablet form—in most cases each tablet contains 0.5 gram ( $7\frac{1}{2}$  gr.). The habit of prescribing in grams should be cultivated; in instructing patients or nurses, the dose to be given four-hourly should be stated in grams as well as by the number of tablets. Whenever charts are employed the nurse should be instructed to record each dose at the time of administration, writing in the daily amount in grams in some contrasting colour, to permit simple calculation at any time of the total amount of drug administered. Many serious accidents have arisen owing to the doctor being under the erroneous impression that the drug had been stopped.

The tablet should always be broken up into small fragments and taken into the mouth with two or three ounces of water or milk. If insufficient fluid is given, the patient will often be found to have a large amount of undissolved drug in the mouth.

The dosage schedule shown in the accompanying table is one which we have found effective for the treatment of most infections. Certain par-

ticular exceptions will be indicated later. We see no reason to recommend varying doses for mild, moderate or severe infections. When it has been decided to employ the drugs we feel that it is unwise to administer less than the suggested initial and subsequent dose, since, in the majority of acute infections, there are few reliable prognostic guides which can enable the clinician to assess the severity of the infection with any accuracy. It is easy to be misled by the apparent beneficial effect of small doses in an occasional case, and to forget that the body could, under favourable conditions, overcome by itself small infecting inocula even in pre-sulphonamide days.

DOSAGE SCHEDULE FOR SULPHANILAMIDE, SULPHAPYRIDINE,  
SULPHATHIAZOLE, SULPHAMEZATHINE AND SULPHADIAZINE

Age Group Years.	Initial Dose.	Four-hourly Dose.	Maximal Treat- ment Course.
Over 5	2.0 to 4.0 gm.	1.0 gm.	60 gm.
2—5	1.0 gm.	0.75 gm.	45 gm.
1—2	0.5 gm.	0.5 gm.	30 gm.
0—1	0.5 gm.	0.25 gm.	15 gm.

Sulphamerazine is rather slowly excreted. This permits a lengthening of the interval between doses. After an initial dose of 3 to 6 gm. the drug may be administered in 1-gm. doses at eight-hourly intervals.

The following general advice regarding dosage should always be followed. First, we consider it wise to insist upon administration of the drugs at four-hourly intervals, especially during the initial forty-eight hours of treatment. Even during the night it will usually be found easy to adhere to this rule in the great majority of infections, where, in the early stages at least, sleep is often disturbed. In the second place, we would suggest that the treatment course should be planned. The doses suggested above can be continued for a complete treatment, which as a general rule should not exceed ten days. This length of time should in fact be regarded as the maximum duration of therapy. In most infections the drugs can be discontinued after the temperature has remained normal for two to three days. Our experience would suggest that such a ruling would cause treatment to be discontinued in most cases before the end of the first week; and it should be remembered that the danger of toxic effects increases as therapy is prolonged. Finally, we see no necessity for decreasing, over a period of several days, the daily amount of drug given. For some time it has been our custom to maintain full dosage until two or three days of normal temperature have been maintained and then to stop further administration.

When prescribing these drugs it is desirable to observe three simple rules: (1) they should be administered four-hourly and each dose should be charted; (2) each dose should be suspended in an alkaline mixture containing 20 gr. (1.2 gm.) each of sodium bicarbonate and sodium citrate; (3) a pint of fluid should be taken between each dose.

There is at present an undoubted tendency to prolong treatment unduly. In a limited number of clinical conditions a prolonged course of treatment may be adopted, but it should only be entered on after a careful considera-

tion of the individual patient. In certain forms of meningitis and in cryptogenic septicæmias, for example, prolonged therapy may be necessary to hold a local focus at bay until the general condition of the patient warrants surgical interference. Even in such cases, however, the most persistent sulphonamide therapy cannot hope to eradicate the local infection, and the sooner it is dealt with surgically the better. In a few conditions prolonged therapy would seem sometimes to have borne fruit—such as the treatment of subacute bacterial endocarditis, or the prophylaxis of streptococcal exacerbations of chronic rheumatic fever. With these few exceptions, it will be found that a relatively short intensive course is greatly to be preferred. Where possible, it should be remembered that the best control of treatment is bacteriological examination, for example, of spinal fluid, blood or sputum. Persistence of the infecting organism should suggest the necessity for increasing the four-hourly dose. A change of drug has sometimes proved valuable.

*Note 1. Dysentery.*—Sulphaguanidine, sulphasuxidine and phthalylsulphathiazole are used exclusively for the treatment of infections of the bowel. Since relatively little is absorbed into the blood stream it remains mainly in the bowel, where it may exert its action upon pathogenic organisms. Its main application is in infections due to the dysenteric group of organisms, but its use in chronic ulcerative colitis has been recommended. Relatively massive doses may be used with complete safety. For infants and young children three to six grams daily can be given; for adults double this dose is desirable. Doses of 18-24 grams daily have been administered to adults with no ill effect, and there should be no hesitation to use such large doses in severe cases for the first day or two. Treatment should be begun as soon as possible, and should be continued for a week after the disappearance of symptoms. A long course of treatment is of little danger here; and since the benefit of treatment lies as much in the eradication of convalescent and chronic carriers as in the treatment of the acute stage, prolonged therapy is desirable.

*Note 2. Urinary Infections.*—Reference has already been made to the concentration of the drugs which takes place in the kidneys. As a result the levels of drugs which are found in the urine are very high, so that the drugs may here exert a direct bactericidal effect. In order to secure therapeutic concentrations in the urine it is not, therefore, necessary to administer the large doses required for the treatment of general diseases. It is unnecessary to exceed 3.0 grams per diem: four doses of 0.5 gram during the day and 1.0 gram before bedtime will usually be found satisfactory. This dosage does not apply to gonococcal infections (see p. 200). Further details must be sought under the section dealing with urinary infections (see p. 788), for it must be remembered that an accurate bacteriological diagnosis is a necessity.

**Parenteral Administration.**—This is of particular importance in those infections which have previously carried high fatality rates, and where, only too frequently, treatment must be begun after the patient has become unconscious. In certain cases it will be necessary to enhance oral administration. Meningitis particularly may be cited: high initial dosage should ensure the early appearance in the cerebrospinal fluid of adequate concentrations of the sulphonamide.

*Sulphanilamide.*—The rapid absorption of sulphanilamide from the bowel makes parenteral administration rarely necessary. Sulphanilamide

L.S.F. (15 per cent.) (Burroughs Wellcome & Co.) or Sulphanilamide Solution (2½ per cent.) (Evans, Lescher & Webb) may be used. As these preparations have the advantage of being non-irritant to the tissues they can be injected subcutaneously, intramuscularly or intravenously. No special precautions are required.

*Sulphathiazole, Sulphadiazine, Sulphamezathine and Sulphamerazine.*—These drugs are sufficiently soluble for parenteral administration only in the form of their sodium salts. Such solutions are exceedingly alkaline, and are thus very irritant to the tissues. Deep intramuscular injection is permissible in the treatment of dangerously-ill patients too collapsed for intravenous therapy: such injections are attended, however, with some risk of serious sloughing of tissues at the site of injection. The best and safest route for the injection is intravenous, and this is the only method of administration which we use. These preparations *must not be injected subcutaneously or intrathecally.*

The materials available are:—

Sodium sulphathiazole: sodium sulphadiazine:

Sodium sulphamezathine: sodium sulphamerazine.

Ampoules contain 1.0 gm. of dry powder; dissolve in 10 c.c. distilled water or normal saline.

An excellent alternative is soluthiazole (M. & B.), which is supplied in rubber-capped bottles ready for use. 5 c.c. is equivalent to 1 gm. of sulphathiazole. The injection should be made slowly. Soluthiazole is neutral and can be safely injected intramuscularly.

**Local Application.**—*Ointments.*—A salve containing sulphanilamide or sulphathiazole has been found of value in the treatment of infectious skin diseases. The drugs may be incorporated in a strength of from 3.5 per cent. Such ointments, however, should not be used without the most careful consideration, for their prolonged use has led to the most severe forms of sensitization dermatitis, which can prove very intractable.

*The Pure Drugs.*—The bacteriostatic action of the drugs has justified their use on burns or into wounds as a powder or pack. There are no serious contraindications to such a method of administration, and in many cases it has resulted in marked benefit. Three points, however, should be noted. First, only pure, sterile drugs should be applied, for the use of unsterilized powder is dangerous.<sup>1</sup> In the second place, the amount of the drug used must be known and should not exceed 10 gm. at any application. As the drugs are absorbed from the wound surface, they may give rise to the same toxic effects as are observed after oral administration. Finally, their beneficial action is maximal if they are applied within a short time (4-6 hours) of wounding. They will have little or no effect on wounds already heavily infected.

Many of the drug firms now supply pure sterile powder in ampoules containing 10 gm. of the drug; in some cases in combination with zinc oxide. Sulphanilamide and sulphathiazole are the two substances most frequently used. Sometimes these compounds are combined (three parts of

<sup>1</sup> Small quantities of the powdered drug may be sterilized in the following way. Into a bottle with screw cap and rubber liner place 10 gm. of powder, and screw the cap tightly. Place in an autoclave or steamer at 15 lb. for half an hour. The powder must not cake or be unduly discoloured.

sulphanilamide to one part of sulphathiazole), since sulphanilamide alone, on account of its greater solubility, may be too rapidly washed out of the tissues. *The tablets of the drugs as used for oral administration must never be used for local application.* The powder should be sprinkled or dusted on to open wounds or inserted and "massaged" into wound cavities. Care should be taken to prevent caking of the powder. The wound is finally covered with moist gauze.

### PROPHYLACTIC

There are various indications for the prophylactic use of these drugs. In the first place, there are conditions in which their use is always justifiable. Two examples which commonly arise may be mentioned: the post-partum case in which there has been considerable interference; and the patient, already suffering pre-existing disease, in whom the extraction of tonsils or of teeth with apical abscesses is contemplated and the occurrence of bacteræmia feared. Here treatment should be bold, and the dosage used should be similar to that advocated in the previous section. Sulphadiazine or sulphathiazole are the drugs of first choice. Treatment should, if possible, begin twenty-four hours before the operation; if not, a single intravenous injection (see p. 76) equivalent to 2.0 gm. of the drug should be given at the earliest opportunity thereafter. Administration should continue for a further minimal period of two days: where a site of potential infection still exists—as in the puerperal case—it is wise to persist with treatment for a total period of seven to ten days.

In many infectious diseases (more particularly when a number of cases are treated in the same room or ward) streptococcal and pneumococcal complications such as otitis media and broncho-pneumonia are liable to occur; the routine administration of sulphonamides has been advocated with a view to their prevention. These complications arise either early, as part of the initial infection, or, more commonly, during convalescence when they are due to cross-infection from some neighbouring patient. Now the beneficial action of the drugs is limited to the period of administration; so that, to prevent such occurrences, all cases would require to receive a sulphonamide during the whole period of susceptibility. Where this is short, as in measles, administration of sulphathiazole or sulphadiazine (according to the therapeutic scales of dosage) for a period of seven days from the appearance of the rash will greatly diminish the occurrence of otitis media and secondary broncho-pneumonia. In diphtheria, too, the use of these drugs after tracheotomy or intubation has almost eliminated broncho-pneumonia, which in the past sometimes proved such a serious post-operative complication. But in scarlet fever and whooping-cough, where the period of susceptibility is much longer, the routine use of the drugs has not in our experience proved justifiable. In such cases a careful watch for the earliest manifestations of otitis media or pulmonary catarrh is to be preferred: sulphathiazole should then be given in full therapeutic dosage. Finally, the possibility of inhibiting the streptococcal exacerbations in such cases as rheumatic endocarditis may be mentioned. American writers, in a carefully controlled clinical experiment, have reported that the use of two doses of 0.5 gm. daily diminished the frequency of rheumatic recurrences. The treatment was continued throughout the winter months

when recurrences are most frequent. Such a use of the drugs cannot be whole-heartedly commended unless the physician is prepared to observe the patient with great regularity.

### TOXIC EFFECTS

Much nonsense has been written on this subject and much unnecessary apprehension thereon has led to inadequate dosage being employed. Considering the widespread use of the sulphonamide series, the total quantity of toxic reactions of importance is remarkably small. Having said this we must equally warn the practitioner that there are definite and serious effects calling for the immediate cessation of all drugs of the series and demanding in some instances prompt counter measures. The basis of all serious toxic effects is sensitization of the body to the sulphonamide employed. Few of the main systems of the body are immune, but it will be of more practical help if we discuss the toxic effects under certain broad headings.

**Common, but of Little Importance.**—*Malaise.*—It will usually be found that the drugs give rise to a general drowsiness or lowered mental acuity, often accompanied by a feeling of malaise. Restlessness, loss of appetite, shallow breathing and inability to concentrate will also occasionally be noted. In some infections the drowsiness is no disadvantage; and in erysipelas and pneumonia, for example, the need for sedatives is now less than in pre-sulphonamide days. Such toxic effects may assume importance when the drugs are given to ambulant patients. The patient should be warned of the possibility and should avoid undertaking any occupation which demands mental concentration and clearness.

*Cyanosis.*—Apart from cyanosis which may be due to the disease, this occurs with nearly all of the drugs, although it is much less noticeable when sulphathiazole and sulphadiazine are used. Its incidence is greatest with sulphanilamide, and in the dosage we have suggested it will be observed in from one-third to one-half of the cases. This should be regarded as a natural accompaniment of sulphanilamide therapy. It is of no moment: the patient (and his relatives) may be reassured and the administration of the drug continued. In many cases methæmoglobin can be demonstrated spectroscopically, but in some the cyanosis seems to be due to the elaboration of pigments from the drugs themselves. With both of these the oxygen-carrying capacity of the blood is unchanged. Very rarely sulphæmoglobinæmia develops, and this more serious change will be referred to later (see p. 83).

*Vomiting.*—Vomiting is most frequently encountered when sulphapyridine is used and we know of no method of preventing its occurrence. If the equally effective preparations, sulphathiazole or sulphadiazine, are used, vomiting will be rarely observed. In itself it is more annoying than dangerous. But it should, however, never be disregarded, because it may make the patient so miserable that he becomes quite uncooperative, and results in the loss of an unknown amount of the drug. In such serious infections as meningitis and pneumonia, therefore, the occurrence of vomiting should occasion an immediate change of drug. If vomiting persists despite this change, absorption of the drug should be ensured by parenteral



administration. It should be remembered that vomiting will probably continue even although the drug is not given by mouth.

**Less Common, but demanding Care.**—*Sensitization.*—Under this general heading may be placed drug fever with or without the appearance of a skin rash. Although these may constitute the main manifestations we would emphasize that sensitization involves a generalized humoral and tissue reaction. All organs are involved and the heart especially should always be examined carefully in older patients. In our experience sensitization occurs in three main forms. *First:* The administration of a single dose may cause the appearance, four to twelve hours later, of a generalized fine maculo-papular rash often accompanied by high fever. Such an occurrence suggests that the patient has, on some previous occasion, received a drug of this series to which he has become sensitive. We have on some occasions continued treatment under these conditions successfully. We have, however, made it a practice under these circumstances to carry out daily examinations of the red and white blood cells. Rather less frequently an apparent prolongation of primary pyrexia may be encountered which may be similarly explained on the same basis. This should call for a careful clinical examination to determine whether the original infection has been brought under control. *Second:* In many cases the original fever will subside in two to three days, to be followed, on the fifth or sixth day, by a reappearance of pyrexia. In this group the occurrence of a rash is less usual. These cases constitute one of the real problems of clinical management, for it is often difficult to exclude a possible recrudescence or relapse. In some infections (for example, cerebrospinal fever and pneumonia) examination of the cerebrospinal fluid, the blood or the sputum may show an absence of the primary infecting organism. This would suggest drug fever as the possible cause. It cannot be too greatly stressed that the most careful clinical survey of the case should be made before the drug is prematurely stopped, especially when the drugs are being used in such conditions as septicæmia and meningitis, which formerly carried high fatality rates. *Third:* By far the most common form of drug rash or drug fever occurs about the tenth day of treatment. The fever may reach 100°-102° F., and remains high so long as the use of the sulphonamide is continued. Even after the drug is stopped it may be two to three days before a normal temperature is reached. The rashes vary in character, but in the most common form, the elements consist of small, rose-red, maculo-papules which fade on pressure. Conjunctival congestion often serves to increase the similarity to rubella or measles. The distribution is widespread, but tends to be more profuse on the extensor aspects, especially in the neighbourhood of the joints. It is frequently very irritable. We have not seen any predilection for skin areas exposed to sunlight.

This complication will be encountered most frequently when therapy has been prolonged, and the possibility of its occurrence forms the strongest argument in favour of the avoidance of lengthy treatment. Sensitization may also be encountered as a result of the sulphonamide treatment of some previous infection. We have seen the subsequent administration of half a gram of one of the drugs give rise to a most severe and acute reaction accompanied by high fever, rigors and generalized rash.

It is not possible to lay down hard-and-fast rules as to the action to be taken when such untoward effects occur. Each case must be judged on its

own merits. We would suggest that the sooner the initial course of treatment is stopped the less risk is there of toxic reactions immediately, or from subsequent treatment for some other infection. A recent survey of cases treated with different sulphonamides did not indicate that the condition was becoming more frequent. It may be that personal idiosyncrasy plays a part in its production.

*Renal Irritation.*—Sulphanilamide, which is the most soluble of the sulphonamide group, has not in our experience been a cause of renal damage. It has in fact been given to patients suffering from acute nephritis without untoward effect. On the other hand, the very low solubility of sulphapyridine and its congeners, and especially of their acetylated portion, means that renal irritation is an ever-present danger. A morning specimen of urine should be examined microscopically on the third or fourth day of treatment. This is of particular importance if the patient has been unconscious, sweating profusely, or if it is suspected that the fluid intake has been low. The occurrence of microscopic hæmaturia must be regarded as the "yellow light," which indicates that caution is required. It is not, in itself, sufficient reason for immediately stopping treatment. In fact, if prompt measures are taken, treatment may be continued with full dosage and the hæmaturia disappear. The measures to be adopted are fortunately simple: the administration during the next twelve hours by mouth of a *minimum* of one pint of bland fluid for every gramme of drug in the daily dose. In addition to this the urinary output *must now be measured accurately*. During the ensuing twenty-four hours a *minimum* of fifty ounces must be passed.

Obvious gross hæmaturia is but an exaggeration of the previous complication. Treatment should be stopped for twelve hours, during which time the patient must absorb, by mouth or other route, a minimum of six pints of fluid. Sodium bicarbonate (2-4 gm.) should be given by mouth. In infections where the drugs have proved life-saving, treatment may then be restarted; repeated microscopic examination of the urine is now imperative, and an accurate record of urinary output must be kept. Should this not exceed fifty ounces in the next twenty-four hours the drug must be stopped.

In conclusion, three points may be emphasized. Although it is often difficult to apply the maxim that "prevention is better than cure," in this instance its application is simple. Hæmaturia will be avoided if the practitioner instructs the attendants to measure the amount of fluid given to the patient, insisting upon a minimum amount of three-quarters to one pint every four hours; and also to insist upon the collection and measurement of all urine, ensuring that a minimal amount of fifty ounces is passed in the twenty-four hours. These rules are frequently disregarded because the drugs are so often used without mishap for a day or two in mild infections, but in severe infections, where the patient is drowsy or uncooperative, strict adherence to them will avoid what can develop into a serious complication.

In the second place, it has been shown that an important factor in keeping the drugs in solution is to make the urine alkaline, although this is not always easy in febrile patients. The administration of alkalis has been advised for other reasons, but we feel that their main value lies in keeping the *p<sub>H</sub>* of the urine as high as possible; the drugs are more soluble in an alkaline medium.

A third point may be noted. With high dosage, crystals of the drugs

will often be seen in urine after it has stood for some time. Provided the urinary output is normal, their presence is of no clinical significance.

**Rare but Important.**—*Urinary Suppression.*—As has been said, hæmaturia arises from the irritation of the urinary tract by the deposition of sulphonamide crystals; should crystallization become excessive, actual blockage of the renal collecting tubules, the pelvis of the kidney or the ureters may occur, giving rise to a mechanical stoppage of urinary flow. This complication has already proved fatal in a few cases. The occurrence of anuria or marked oliguria necessitates immediate cessation of the drugs. To begin with, fluids by mouth must be forced, and the intravenous injection of one pint of sterile normal saline solution should be given. Unless urinary flow recommences very quickly (within 4-6 hours) further excessive administration of fluids is unwise; this will only lead to generalized œdema or to œdema of the lungs. Such a case may require specialist surgical assistance; ureteric catheterization with the instillation of warm alkaline solution has been carried out successfully in some instances.

*Blood Dyscrasias.*—When the toxicity of the sulphonamides is discussed, attention is usually focussed upon this group of complications. In an experience, however, of several thousand cases treated with the drugs, they have only been seen by us on a few occasions. For this reason we are inclined to emphasize again that the probability of their occurrence is increased by careless use of the drugs over long periods.

The conditions which have been encountered include purpura, with or without an acute hæmolytic anæmia; acute hæmolytic anæmia with or without bone marrow hypoplasia; and granulocytopenia or agranulocytosis. A peripheral disturbance of the blood elements may be the essential feature in some cases; in others hypoplasia, or aplasia of the hæmopoietic tissues, results. Although commoner after a prolonged course of therapy, such changes have occurred during the first five days of treatment and after comparatively small dosage. In this group of cases personal idiosyncrasy may play a large part in their causation.

In regard to the clinical recognition of these effects little need be said in this section. The occurrence of unexplained fever has been recorded as often preceding their onset. A slight degree of jaundice, especially of the sclera, is a valuable warning signal which should demand a complete blood examination. A complaint of sore throat by a patient who has been receiving one of the drugs for more than a week should always suggest the possible beginning of an agranulocytosis. The occurrence of these blood disorders is an absolute indication for stopping the drugs. It is possible that the danger of their occurrence is increased if the patient is anæmic at the outset of treatment. The administration of the drugs to persons already suffering from some upset of the hæmopoietic system demands daily examination of the blood cells.

The further treatment of anæmia differs in no respect from that of similar forms of anæmia due to other causes, and reference should be made to p. 461. The treatment of agranulocytosis is discussed on p. 513.

The prevention of such complications is often difficult, for they may occur with startling suddenness. The occurrence of some other toxic effect such as a drug rash or drug fever should never be disregarded, especially if in such a case further treatment is thought necessary. We would advise that when it is decided to continue treatment for more than eight days,

examinations of the hæmoglobin and of the white blood cells must be made regularly. Should the hæmoglobin fall below 40 per cent. (Sahli) or the total white cell count be under 3,000 per c.mm., treatment must immediately be discontinued.

*Sulphæmoglobinæmia.*—This complication has arisen in a few patients who were receiving sulphanilamide. Since the change is irreversible, the oxygen carrying capacity of the blood is impaired. In our experience, the occurrence of sulphæmoglobinæmia has been accompanied by a severe degree of cyanosis, shallow, almost imperceptible respirations and a rapid pulse of thin quality. The patient looked exceedingly ill, and there was no hesitation in stopping the drug. Recovery was uneventful but very slow; cyanosis of an obvious degree was still present three to four weeks later. It has been suggested that this toxic effect is due to the absorption of sulphides from the large bowel, especially if the bowel contents were very fluid. The use of purges which give rise to watery stools (for example, magnesium sulphate) is, therefore, inadvisable when the patient is receiving sulphonamides. It is now known that the earlier restrictions placed upon the use of sulphur-containing foods such as eggs and onions are unnecessary.

*Peripheral Neuritis.*—Such cases are rare. We have not seen an undoubted case. The administration of the drugs must be stopped at once.

### SULPHONAMIDES AND PENICILLIN

The advent of penicillin makes it necessary to consider under what circumstances penicillin or the sulphonamides should be chosen as the chemotherapeutic agent. Broadly speaking, comparison of the two brings out three major differences. First, penicillin is much more active against most staphylococcal infections; second, penicillin is almost devoid of toxic side-effects; and third, it is effective even when pus has been formed. These three considerations constitute the main deciding factors in choosing the method of treatment and they may be discussed under the following headings:

*Bacteriological.*—It will be unusual for the practitioner to have foreknowledge of the infecting agent when treatment is first considered. Full sulphonamide therapy should be begun at once, but only after all necessary specimens for bacteriological examination have been taken, *e.g.*, blood culture, lumbar puncture, swabs, etc. Unless there is good reason to suspect a staphylococcal infection the effect of sulphonamide therapy should be observed for 24 hours. By this time the results of bacteriological examination will usually be available and further treatment may be decided accordingly.

So far as individual bacteria are concerned, it can now be stated that pneumococcal pneumonia reacts as well to sulphonamides as to penicillin. Meningococcal infections respond more rapidly to sulphonamide therapy, so that penicillin should never be relied upon solely.

*Fear of Toxic Side-Effects.*—Especially among the older age-groups, patients will be encountered in whom the presence of previous disease or degeneration adds to the hazard of sulphonamide therapy. In a dehydrated patient or in the person with chronic cardio-vascular or renal disease, the ability to excrete sulphonamides adequately may be questioned, and in such circumstances penicillin should be preferred. Again, previous sensitization to the sulphonamides may be known to have occurred and penicillin will then prove the safer drug. Occasional patients are encountered in whom

vomiting forms a serious drawback to adequate sulphonamide therapy. An initial period of full penicillin dosage may overcome the difficulty.

*Development of Pus.*—When a purulent complication is already present, the exhibition of sulphonamides is valueless. In such cases the administration of penicillin not only systemically but also into the abscess is often completely effective. The same holds true when a purulent complication develops during the course of sulphonamide therapy; the sulphonamide should be stopped and penicillin substituted.

### GENERAL CONSIDERATIONS

The tendency for the indiscriminate use of the sulphonamide drugs is widespread: this is mainly due to a lack of understanding on the part of the user of what the drugs can do. By this we do not mean a knowledge of the precise mode of action of the sulphonamides, for in truth our knowledge of this is still of a fragmentary nature. But we do feel that certain broad deductions can be drawn from clinical experience which have a general application, no matter in what diseased condition the drugs may be used.

To begin with, it is inaccurate to think of the drugs as "antiseptics." Although their action is an antibacterial one in the broadest sense, they must not be regarded as substances which merely "kill bacteria." In fact, their action in this respect is poor when compared with many commoner germicides. Experimentally, it has been shown that the drugs "interfere" between the bacterium and some substance normally present in the tissues which is essential for its metabolism and reproduction. As a result, the scales are weighed against the invader, and the natural defences of the host may then cope with it satisfactorily. Certain broad inferences may be drawn from this conception. In the first place, since the effect is upon the growth of the organism, it is essential to administer the drugs as early as possible in any infection in order to introduce the interfering substance while the bacterial population is still small. In some diseases, such as pneumonia, the only hope at present of further improving the outlook is to begin treatment upon the appearance of classical symptoms rather than to await the development of classical signs which will permit a clear-cut diagnosis. In the second place, it is clear that the drugs have no action in stimulating phagocytosis nor in neutralizing any specific toxin which the bacterium may produce. Finally, once the bacterium has become shut off within a septic focus, it is unlikely that any sulphonamide will sterilize the local purulent collection. The administration of sulphonamides may, it is true, prevent further invasion of the tissues from this focal point; but for final and complete recovery its surgical eradication will be necessary.

These points are worth emphasizing. The recovery of the patient who has received sulphonamide is often thought to result from the mere interaction of two forces—the bacterium and an antibacterial substance. We would prefer to depict chemotherapy with sulphonamides as resting upon a triple base, the drug, the bacterium and the host, each limb of the tripod having an importance as great as the other two; so that weakness in one may well prevent beneficial action.

**The Drug.**—It is probable that there are effective ranges of blood concentration for each of the different drugs. The evidence is not conclusive, but it seems wise to try to achieve rapidly a fairly high concentration of

drug in the blood stream and to keep that concentration at a steady level during the period of main attack. We believe that once the decision has been made to use the drugs, no advantage is to be gained by employing small dosage, and would strongly advocate that all types of case should receive as a minimum the dose suggested herein. Facilities for the estimation of the blood content of the drug are unlikely to be available in general practice for some time yet; but in our experience, using the doses advised, there will be few occasions when such knowledge will prove of much assistance. The practitioner need have little fear of untoward effects from a short intensive course of therapy provided he follows the general principles which we have outlined.

**The Bacterium.**—Bacteria undoubtedly vary in their susceptibility to the action of the sulphonamides, both as between different families and as between different strains of the same family. In respect of families it is perhaps easier to list those upon which no action has been proved. These include the typhoid group, *B. tuberculosis*, *B. abortus*, and almost all virus infections. But even in those families which are as a rule susceptible, strains have now been isolated which seem able to grow in dilutions of the drugs usually inhibitive to other members of the group. Apart from the obvious importance of this in the direct transmission of gonorrhœa, too much emphasis may be attached to these strain differences. In our clinical experience of medical cases such bacteria are still met with very rarely. Wherever possible, the course of the disease should be controlled by bacteriological examination, particularly in cases of meningitis and septicæmia. It is important to remember in this connection that the presence of sulphonamides in pathological fluids may have the effect of inhibiting bacterial growth. *The bacteriologist should, therefore, be warned of the fact that the patient is receiving sulphonamides so that he may supply the special culture medium required.* This contains 2.5 mg. per cent. of *p*-amino-benzoic acid, a substance which neutralizes the inhibiting effect of a sulphonamide, and permits bacterial growth in its presence. If this chemical is not available, the injection under strictly aseptic conditions of a little procaine (two or three drops) into the culture medium will serve. Since procaine is an antagonist of the sulphonamides, it should be used sparingly as a local anæsthetic on cases receiving the drugs.

Finally, since in some cases bacteria disappear with great rapidity after sulphonamides have been administered, any specimens required for bacteriological examination should be taken before therapy is instituted. If this is not done, it will often be impossible, twenty-four hours later, to establish the correct diagnosis.

**The Host.**—The host's reaction to the infection, *ab initio*, is undoubtedly of the greatest importance. If resistance is poor, then sulphonamides may well fail. In this respect, attention must be paid to the apparent failure, in pneumonia and cerebrospinal fever, of a combination of chemotherapy with specific serotherapy. It suggests that those who now die do not die from any lack of specific antibodies. It may perhaps indicate that what is lacking is some non-specific or tissue resistance. The sulphonamides are no panacea; they require for effective action every form of ancillary treatment—efficient nursing, good diet, and all that is implied by careful clinical supervision throughout the disease.

T. ANDERSON.

W. R. SNODGRASS.

# THE CLINICAL USE OF PENICILLIN

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**F**EW drugs have been so carefully introduced to medical therapeutics as penicillin. The facts of its nature and the methods of its use have been clearly worked out, and though certain features require clarification the practitioner should no longer feel perplexed or appalled at the prospect of administering penicillin to the patient. There is no need to describe again how Fleming in 1929 first noticed the action against *staphylococcus aureus* of the broth on which the fungus *Penicillium notatum* was growing; and of how Florey and his associates in Oxford succeeded in 1940 in extracting the active principle from the growth medium. Suffice it to say that there has been put at our disposal one of the most satisfying drugs in medicine; for there is nothing fortuitous in the action of penicillin, and in its presence the sensitive organisms are bound to disappear. Indeed, if they do not disappear the fault probably lies not so much in penicillin as in our method of using it.

A practical method of producing penicillin by synthesis has not yet been achieved, but this is of little consequence because the manufacturing chemists are now producing penicillin in vast quantity and admirable purity by growing the mould in deep vat cultures, and the drug is readily procurable at reasonable price on a doctor's or dentist's prescription. Penicillin has such unique and remarkable properties that there is no longer justification for withholding it in susceptible infections. Accordingly it is essential that the practitioner should be familiar with its therapeutic use.

There is nothing particularly difficult about using penicillin provided three facts are remembered: (1) it is a true chemotherapeutic drug; *i.e.*, it is a chemical substance which, when introduced into the tissues, will act specifically against invading organisms without at the same time damaging the cells of the host; (2) it is selective in its action; with certain exceptions, gram-positive micro-organisms are within its range and gram-negative bacilli are resistant; (3) it is an unstable drug when in solution; in dry powder form it retains its potency.

## CHEMISTRY

For therapeutic purposes penicillin is regarded as a single substance, but there are at least four forms of the drug differing slightly in their chemical constitution. These four variations have a common organic acid nucleus and a side-chain characteristic for each form. They are known in Britain as Penicillin I, II, III and IV, and in U.S.A. as Penicillin F, G, X and K. The four penicillins are active against the same type of organisms, but minor differences in their activity and stability have been noted. The products on the market consist mainly of Penicillin II with small amounts of Penicillin III or IV. Pure Penicillin II, produced by crystallization, assays at 1,660 units per milligram. The potency of the original penicillin used by the Oxford workers was only in the region of 20 units per mg., the rest

of the product being impurities. Commercial penicillin is now very much purer, and usually contains about 1,400 units per mg.

A clinical dosage of 100,000 units may sound enormous, but it represents only about 1 grain (60 mg.) of pure penicillin. The unit was originally devised by the Oxford workers as an artificial measure of bacteriological activity, before the chemical formula had been discovered. An International Unit has been adopted; it is the activity of 0.6 micrograms of the International Penicillin Standard, a specimen of pure crystalline sodium salt of penicillin. The International Unit is approximately equivalent to the Oxford Unit.

### ABSORPTION AND EXCRETION

Penicillin penetrates most tissues with great ease and rapidity. It is absorbed quickly, but unfortunately it is excreted just as readily by the kidneys. Following intramuscular administration penicillin immediately diffuses from the site of injection, and a maximum concentration is found in the blood within thirty minutes. Thereafter, the blood level falls sharply as the substance is excreted. A considerable proportion of the dose can be recovered from the urine, while a certain amount is inactivated in the body. To maintain continuously an inhibitory level of penicillin in the blood and tissues, doses must be given at intervals which are sufficiently frequent to allow for the rapid excretion of the substance.

Certain body membranes are relatively impermeable to penicillin. It passes only in minute amounts through the blood-brain barrier of pia-arachnoid, the pleura, pericardium and peritoneum, and joint membranes. Similarly, if penicillin is injected locally into the space within these membranes a reservoir is formed from which the substance is slowly absorbed, and therefore less frequent injection is required.

**Mode of Action.**—At first it was thought that penicillin exerted its effect by bacteriostasis: the organism was not killed but simply arrested in its development so that it died out or was overcome by the body's resistance. It is true that bacteriostasis does occur in certain circumstances; but it has now been shown that in adequate dosage the drug is bactericidal, preventing the oxygen uptake of growing bacteria. The object of treatment must be to maintain adequate concentration of the drug in the tissues until all the sensitive organisms have been destroyed.

### SENSITIVE AND INSENSITIVE ORGANISMS

<i>Sensitive</i>	<i>Insensitive</i>
<i>Streptococcus hæmolyticus.</i>	<i>B. typhosum.</i>
<i>Streptococcus viridans.</i>	<i>Salmonella paratyphi.</i>
<i>Streptococcus anærobic.</i>	<i>Shigella dysenteriæ.</i>
<i>Diplococcus pneumoniae.</i>	<i>B. coli.</i>
<i>Staphylococcus aureus.</i>	<i>Ps. pyocyanea.</i>
<i>Staphylococcus albus.</i>	<i>B. proteus vulgaris.</i>
<i>Neisseria gonorrhœæ.</i>	<i>Hæmophilus influenzae.</i>
<i>Neisseria meningitidis.</i>	<i>Hæmophilus pertussis.</i>
<i>Bacillus anthracis.</i>	<i>Brucella melitensis</i> and <i>abortus.</i>
<i>C. diphtheriæ.</i>	<i>Monilia albicans.</i>
<i>Actinomyces bovis</i> (variable).	<i>Past. pestis; Past. tularensis.</i>



SENSITIVE AND INSENSITIVE ORGANISMS—*continued*

<i>Sensitive</i>	<i>Insensitive</i>
Cl. tetani.	Mycobacterium tuberculosis.
Cl. welchii.	Blastomyces.
Cl. septicum.	Most viruses.
Borrelia vincenti (Vincent's angina).	Toxoplasma.
L. icterohæmorrhagiæ.	Plasmodium vivax.
Tr. pallidum (syphilis).	Trypanosomal infections.
Tr. pertenue (yaws).	Leishmanias.
Borrelia novyi (relapsing fever).	

Variations in sensitivity are noted in different strains of certain organisms, *e.g.*, streptococci and *C. diphtheriæ*. And some organisms that are normally sensitive to penicillin occasionally prove to be resistant. About 5 per cent. of staphylococci appear to be inherently resistant to penicillin, though some become sensitive to very high dosage. Insensitive strains can be developed *in vitro* by exhibiting them to minimal doses of penicillin, but fortunately this does not seem to be a feature of clinical application. Fortunately also, organisms that are penicillin-resistant are not necessarily sulphonamide-resistant, and *vice versa*, for the mechanism of resistance to the two drugs appears to be different.

## STABILITY OF PENICILLIN

Penicillin is an acid, but it rapidly loses its activity in acid form, and is supplied for clinical use in the form of its sodium or calcium salt. The salts are equally efficacious, but calcium penicillin is less hygroscopic and is therefore easier to handle and less liable to deterioration. Even in the form of its salts penicillin is more liable to loss of activity than other drugs commonly handled in clinical use. It is destroyed by acid and alkali, by the heavy metals such as copper and lead, by alcohols, and by oxidizing agents such as hydrogen peroxide and potassium permanganate. Since most of the common antiseptics fall into one of these categories, penicillin must be used alone. It loses activity when heated above body temperature and should be stored in a cool place. Penicillin is also destroyed by "penicillinase," an enzyme found in many common airborne bacteria such as members of the coliform and subtilis-mesentericus group.

The drug comes from the manufacturers in sealed glass ampoules, and in this dry state it can be stored without loss for at least a year. In aqueous solution penicillin is much less stable and will lose its activity in a matter of days. Solutions for injection should therefore be made up fresh, and should not be kept longer than 24 hours at room temperature, or 4-5 days in a refrigerator.

These various handicaps in using penicillin cause little difficulty in actual practice. They are easily appreciated and remembered, and the practitioner's aim should be only to use for injection solutions of penicillin freshly prepared in sterile water or saline; to avoid using other antiseptics at the same time (though there is no objection to sulphonamides); and to prevent the development of penicillinase in creams and powders by avoiding contamination from the air or from non-sterile instruments.

### DOSAGE OF PENICILLIN

Ideally, the dosage necessary for an individual case is best determined after bacteriological investigation of the infection combined with frequent estimations of the penicillin blood level, but in actual practice these refinements can usually be dispensed with and kept for the exceptional case. In most infections a continuous blood level of 0.1 unit penicillin per c.c. will maintain bacteriostasis, and this level can be secured by 15,000 to 20,000 units every 3 hours by intermittent intramuscular injection, or 100,000 units every 24 hours by continuous intramuscular or intravenous drip. The serum concentration must never be allowed to fall below an inhibitory level: failure to observe this fundamental rule—such as the neglect of regular injections throughout the night—may result in failure of the treatment.

The modern tendency is to give considerably higher doses than the above, firstly because there is evidence that a really high penicillin concentration has a definite bactericidal effect and the organisms can be overwhelmed; and secondly because some relatively resistant organisms can become sensitive in the presence of a high concentration. All the more is it desirable to give high doses when bacteriological control is not employed, and when the infection may be a mixed one. Actual figures of penicillin dosage are still partly a matter of personal opinion, but in most systemic infections the practitioner can feel confident in a régime of 200,000 units as an initial dose followed by 50,000 units every 4 hours.

The importance of the foregoing in the treatment of septicæmic conditions will be appreciated; the blood level must always be saturated. But, fortunately, there is increasing evidence that less frequent injections are permissible in local infections, *i.e.*, where the organisms are confined to localized infected areas and are not circulating in the blood stream. It has been shown that during systemic administration penicillin is present in tissue fluids and wound exudates considerably longer than it remains in the blood stream. Four or five hours after a single injection of 100,000 units there is no longer an adequate concentration of the drug in the blood, but it is invariably present in adequate inhibitory amounts in the wound for 8 hours, and for 12 hours in 50 per cent. of cases. Accordingly, it is justifiable to treat many focal infections by injections of 100,000 units 12-hourly; and in conditions such as cellulitis, early infections of the hand, acute mastitis and others, the results of this twice-daily injection régime are probably as good as those from full systemic dosage.

It is interesting that a patient with nephritis will maintain a penicillin blood-level longer than normal because the kidneys are slow to excrete the drug. Attempts have been made to retard normal renal excretion by simultaneously injecting diotrast or para-aminohippuric acid, but it is not a popular method. A more practical scheme is to provide a reservoir of penicillin in the tissues from which the substance is slowly absorbed. A single injection (100,000 units in 2 c.c.) of a suspension of calcium penicillin in 4.8 per cent. beeswax in peanut oil will provide an adequate blood concentration for 7-10 hours, and a satisfactory blood concentration for 24 hours has been claimed after 600,000 units.

Whatever method of treatment is employed, it must be continued for a

minimum of three days in soft-tissue infections, and for five days in infections of bone. These are bare minimal figures, and the practitioner must be prepared to continue treatment much longer, if necessary for several weeks, and certainly until the temperature has been normal for 48 hours.

This scheme of treatment should suffice for the common acute staphylococcal and streptococcal infections. But in bacterial endocarditis, in syphilis, and in many chronic infections such as chronic osteomyelitis and actinomycosis, dosage must be high and treatment prolonged for the following reasons: (1) there is a variation in sensitivity of different species of micro-organisms; and, though the size of the organism is not the sole criterion, the bigger organisms such as spirochaetes as a rule require higher dosage; (2) there is considerable strain variation even among the same species of organism; (3) the blood supply to the part may be deficient, resulting in a low concentration of penicillin. The problem, as ever, is to get the drug to the part, and if the organisms are shut away in dense fibrous tissue or in sclerotic bone or in vegetations it is necessary to give high doses so that at least some of the drug will reach the affected part.

Thus in the treatment of any given case the guiding principles are clear-cut. The practitioner should ask himself, firstly, what is the organism causing the infection, and how sensitive is it likely to be to penicillin; and secondly, what is the probable state of the blood supply to the affected part. Let him visualize these facts, and, even in the absence of laboratory control, he will not go far wrong.

### SYSTEMIC ADMINISTRATION

Systemic administration is the method of penicillin therapy with the widest application because the drug will be carried to all parts of the infected area, provided the local blood supply is adequate. The most satisfactory method of achieving this is by intermittent intramuscular injection, and the technique is described below. Intravenous injection is equally effective but has no advantage, and has the drawback of causing thrombosis at the needle-site. Subcutaneous injection was objectionable when penicillin preparations were full of impurities, but there is now nothing against it.

For systemic administration by injection either the sodium or calcium salt can be used. The appropriate amount of sterile water or saline is added to the dry powder which is readily soluble. The manufacturers commonly issue the drug in sealed ampoules containing amounts such as 100,000 units, 200,000 units, 500,000 units or 1,000,000 units. If, for example, it is desired to inject 50,000 units 4-hourly, then 4 c.c. of sterile water should be injected into an ampoule of 200,000 units and the first 1 c.c. dose withdrawn. The remaining penicillin, being now in solution and unstable, should be used the same day. Asepsis should be preserved during these manoeuvres. The suitable solvents are sterile distilled water or sterile normal saline. Unless taken from a sealed ampoule, the solvent should preferably be freshly prepared; a solution that has been left standing for some time may contain pyrogenic substances or organisms producing penicillinase.

Ideally the syringe for injection should be boiled and allowed to cool before use, but if it is stored in alcohol little harm should result: any remaining trace of alcohol will not destroy the penicillin during the short time they are in contact, nor will a trace of alcohol on the patient's skin. The needle should be fine and sharp and should be quickly inserted, and the

fluid injected slowly. Some samples will cause pain for a few minutes at the site of injection, and if necessary with a sensitive patient this can be minimized by applying ice to the part beforehand or by adding 1 c.c. of 1 per cent. procaine to the injection fluid. As a general rule the smaller the volume of the injection the less the pain, but with bigger doses, *e.g.*, 100,000 units, it is advisable to dissolve the drug in 2 c.c. of water because 100,000 units in 1 c.c. is a very concentrated salt solution and its injection will be painful.

The technique of administering penicillin in beeswax and oil is somewhat difficult, for the medium is viscid and a large-bore needle is required for the intramuscular injection. The mixture should be gently warmed to facilitate its passage through the needle. It is sufficient to inject 100,000 units in 2 c.c. eight-hourly.

Continuous intramuscular infusion is an alternative method of systemic administration and is very effective. The 24 hours' supply of penicillin (*e.g.*, 100,000 units) is dissolved in 100 c.c. normal saline and delivered by continuous intramuscular drip into the thigh or pectoral muscles. By such means an inhibitory amount of penicillin is always present in the blood stream. To ensure delivering 100 c.c. evenly over the 24 hours a special apparatus such as the Eudrip is required. It works well if properly supervised, but is really only suited for institutional treatment. Strict asepsis is particularly important in continuous intramuscular therapy, for the danger of gram-negative organismal contamination is a real one and a localized abscess at the end of the needle may inactivate the penicillin as it slowly drips into the site. The position of the needle should be changed every 48 hours. And there should be no synthetic rubber in the infusion set, for it inactivates penicillin.

**Oral Administration.**—Penicillin is readily absorbed in the jejunum, but oral administration is an unsatisfactory method because the acid of the stomach largely destroys the activity of the drug. Attempts to neutralize the acid by simultaneously giving sodium bicarbonate or egg albumen give uneven results. Three to four times the normal dose of penicillin is necessary to allow for destruction of the greater part of the drug, and while meantime the oral method is not recommended, further work may show it to have a place in treatment, particularly in achlorhydric patients.

On the other hand, in infants under one month oral administration is the method of choice. The factors which make penicillin unreliable in an adult are not present at this early age: the gastric acidity is low and the jejunum relatively sterile. The dose for premature infants is 5,000 units, and for infants up to one month 10,000 units; this is dissolved in 1-3 c.c. normal saline and added to the first ounce of each milk feed, and the remainder of the feed given immediately afterwards. In breast-fed infants the ounce of milk is expressed from the mother's breast. The mixture is invariably well tolerated. It is a simple and reliable method of administration and is more satisfactory than repeated intramuscular injections in a weakly infant with deficient musculature.

### LOCAL ADMINISTRATION

The topical application of penicillin has distinct advantages over systemic administration for certain types of cases in that a very high concentration

can be brought to the part and the patient is spared repeated injections. The difficulty lies in getting the drug satisfactorily to all the interstices of the infected area, but in open lesions where this can be assured, it is the method of choice. In such cases gram-positive organismal infection should be eradicated by daily or twice-daily treatment for 3-4 days.

One disadvantage of local penicillin treatment is that gram-negative organismal infection supervenes almost invariably. Despite aseptic dressing technique, *B. pyocyaneus*, *B. coli* and *B. proteus* appear as contaminants and seem to flourish in the absence of staphylococci and streptococci. These organisms produce a characteristic thin salmon-pink "gram-negative pus," which is best treated by phenoxetyl or proflavine or by local streptomycin when this becomes available.

**Penicillin Solution** for local application should be made up fresh daily, and a strength of 500 units per c.c. is adequate. It can be applied in various ways: (1) instillations of 2-10 c.c. twice daily through a fine rubber catheter into a sinus or cavity; (2) wet dressings of gauze once or twice daily; (3) spray, for skin conditions, repeated hourly with the part left uncovered; (4) injection into a closed abscess cavity after aspiration of the pus. This can be effective where the abscess is well localized with a distinct wall, e.g., an infected olecranon bursitis; but is usually unsatisfactory in more diffuse abscesses.

As has been stated, serous membranes are relatively impermeable to penicillin, and infections therein are better treated by local rather than systemic administration in order to achieve an adequate concentration of the drug. In *thoracic empyema* the pus should be aspirated every second day and replaced by a smaller volume of penicillin, e.g., after aspiration of all available pus 20-50 c.c. of penicillin solution containing 100,000 units is injected into the cavity. This volume allows the fluid to be dispersed throughout the cavity. It will be found that inhibitory amounts of penicillin are present in the pleural fluid up to 48 hours. Furthermore, with a dose of 100,000 units of penicillin intrapleurally a reservoir of penicillin is formed which is slowly absorbed and will create a significant concentration in the blood for 24 hours. Thus it is unnecessary to give concomitant systemic cover when a high intrapleural dose of penicillin is injected daily. This prolonged action of penicillin within a serous cavity is independent of whether the cavity wall is normal or acutely inflamed. A similar technique and dosage should be used in acute infections in *joints* and in the *pericardium*.

When it is decided to use penicillin in the treatment of *meningitis* and infections of the brain and spinal cord (and it should be remembered that sulphonamides are usually the drugs of choice), it should be given by intrathecal injections in addition to systemic therapy: 10,000 units of penicillin (2,000 units per c.c.) are given by lumbar puncture. One intrathecal injection can maintain an adequate concentration in the cerebrospinal fluid for 24 hours. The injection should not be large in unitage or volume for fear of a meningeal reaction; and strict asepsis, with Zeiss filtration of the penicillin fluid, should be maintained in case a *pyocyaneus meningitis* is produced.

**Powder.**—For local application as a powder, sodium penicillin is unsuitable because it is deliquescent; but calcium penicillin maintains its potency when exposed to the atmospheric moisture and is ideal for local use. It should not be applied undiluted to the lesion, for two reasons: pure peni-

cillin powder can be necrotoxic; and because a vehicle is necessary in order to spread the minute amount of penicillin required over the relatively large area. Micro-crystalline sulphathiazole powder is a suitable diluent, and it is common to employ a penicillin-sulphathiazole powder in a strength of 500 units per gm.

The mixing of the powders can be carried out aseptically by the practitioner or dispensing chemist, and the manufacturing chemists have a penicillin-sulphathiazole preparation on the market. Such a powder retains its potency so long as penicillinase-producing organisms do not infect it. It is usually safe to store it in a glass container or even a light metal insufflator for several months.

The powder should be insufflated daily to form a thick hoar-frost over the infected area, and covered with tulle gras. It is effective on a relatively dry surface such as a granulating wound; an oozing wound will wash away the powder, and to rely on it in such circumstances is to create a false sense of security. The sulphonamide content of the powder may cause a dermatitis in some cases. Lactose has been suggested as an alternative vehicle.

**Creams and Ointments.**—Ointments of calcium penicillin in vaseline or lanoline retain their potency fairly well, but such vehicles do not release their penicillin readily. A more suitable vehicle is 30 per cent. lanette wax in water, which is the usual base for the cream. A penicillin cream of 500 units of penicillin per gram of lanette wax releases its penicillin readily and equably, but as it is an aqueous preparation it will not keep longer than 2-4 weeks.

Ointments, being relatively stable, are marketed by the manufacturing chemists with the constituents already mixed. Creams must be freshly prepared, with strict asepsis; and as they are suitable media for penicillinase-producing organisms they should be kept air-tight and should be dipped into infrequently and only with a sterile instrument.

These preparations should be smeared thickly over the area with a sterile spatula, and covered with gauze. They make a kindly dressing on a raw surface. The penicillin is slowly released and the dressing need only be renewed at intervals of 48 hours. The lanette wax base is inert and needs to be scraped off the wound prior to the fresh application.

**Lozenges and Pastilles.**—Relatively stable preparations are on the market of a lozenge containing 500 units of penicillin. The basis of the lozenge is glucose or sucrose and starch, and they tend to cause glossitis in some cases. Pastilles with a gelatin base are less irritating, but are more unstable and should be made up fresh when required. They are effective in mouth infections, and the patient should always have one in his mouth to suck during waking hours. The indiscriminate use of penicillin lozenges and indeed all local applications of penicillin is to be deprecated since it may encourage the growth of organisms insensitive to penicillin.

**Penicillin by Inhalation.**—Aerosol penicillin, and the Collison Inhaler, work on the principle of air or oxygen bubbling through an aqueous solution of penicillin, producing a fine spray which is inhaled through a mask. The dose for an adult is about 25,000 units in 1 c.c., and this is nebulized and inhaled every 3-4 hours.

The method is of advantage in tracheal and bronchial infections to which it brings a high local concentration of penicillin. Many clinicians are

enthusiastic about inhalation therapy, but others question whether at present it is worth the trouble. The mechanical apparatus and oxygen are expensive, and the hand insufflator is tedious. Frequently systemic therapy will prove to be equally effective, and where local application is specially desirable, as in bronchiectasis, it is practical to instil 100,000 units in 15 c.c. into the bronchial tree through a nasal catheter after cocaineizing the throat.

### REACTIONS TO PENICILLIN

Penicillin is a non-toxic drug, but a small proportion of cases (about 1 per cent.) show penicillin sensitivity. The most common effect is urticaria developing during treatment at about the eighth to tenth day. Being generally of a mild order, it disappears spontaneously in a few days. Occasionally, however, it is severe enough to demand treatment, which can usually be effectively undertaken by the use of the antihistamine drugs (see p. 96).

Transient pain at the site of intramuscular injection has been mentioned. Both pain and urticaria are less common with the purer preparations of penicillin now available. Herxheimer reactions may occur in the treatment of syphilis with penicillin, causing temporary fever, malaise, increase of skin eruptions and swelling of lymph glands (see p. 213).

### SUPPLEMENTARY THERAPY

**Surgical Measures.**—It needs to be stressed that penicillin does not supplant surgery, and that most cases should be treated by orthodox surgery with penicillin as an adjunct. Pus must be evacuated by incision, or in some cases aspiration, and necrotic soft-tissue and bone sequestra removed. Nevertheless, it is frequently justifiable to be conservative in early cases and to delay incision for 24-48 hours. The infection may subside with no other therapy than penicillin, and there is little chance of any serious spread of the infection or septicæmia while it is being administered. In some conditions orthodox surgical treatment has been radically modified. For example, in acute osteomyelitis operative intervention is now contraindicated in the early stages; better results are achieved by waiting and incising the soft-tissue abscess if it develops.

Twenty-four hours after the beginning of adequate penicillin therapy for acute infections the patient usually feels greatly improved; pains disappear, the appetite is restored, and there is a fall in temperature. But while this is usually all to the good, the practitioner should be on his guard against being lulled into complacency, and he should make frequent full reassessments of the case.

**Sulphonamides.**—The activity of penicillin is not reduced by simultaneous administration of sulphonamides or any other chemotherapeutic drug, but there is little if anything to be gained by this type of supplementary therapy. Against infections due to organisms that are sensitive both to penicillin and to sulphonamides entire reliance can be placed in the stronger drug; to add sulphonamide therapy is simply to nauseate the patient and give extra labour to the nursing staff. Similarly, it is foolish to add penicillin

to other therapy in a pure coliform infection. The only indication for combined therapy is in a mixed infection of gram-positive and gram-negative organisms, for example, staphylococci and coliforms. There may, however, be an indication for replacing penicillin by sulphonamides where a staphylococcus or streptococcus is proving to be penicillin-resistant; and sulphonamide therapy is usually preferable in lobar pneumonia and meningococcal meningitis because of the greater convenience of oral administration.

J. S. JEFFREY.



# THE CLINICAL USE OF ANTIHISTAMINE DRUGS

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## INTRODUCTION

THE suggestion by Dale and Laidlaw in 1910 that histamine might be concerned in the production of anaphylaxis and allergy was followed by many attempts to produce a single drug or form of treatment which would counteract these states regardless of their ætiology. In recent years histamine injections, histaminase, histamine azoprotein (Lertigon) have been tried in the treatment of allergy. Of these, the only one which seems to have produced some clinical benefit is Lertigon.

From 1933 onwards French workers had been systematically searching for synthetic antihistamine drugs, but it was not until 1942 that their efforts were crowned with success. In that year Antergan (N-phenyl N-benzyl N-dimethyl ethylenediamine) was introduced and soon the results of its clinical trial began to appear in the French literature. In 1944 neoantergan was introduced in France and in the following year Benadryl and Pyribenzamine in America. Clinical trials of these drugs have shown that they have a place in the treatment of certain allergic states. The search for more potent antihistamine drugs continues, and it may well be that we have as yet but touched the fringe of new developments. New antihistamine drugs are already under clinical trial.

## MODE OF ACTION

A knowledge of the mode of action of this group of drugs is necessary if they are going to be used efficiently. From experimental and clinical studies it appears that their clinical effects are produced by blocking the tissue receptors for histamine. They in no way interfere with normal or abnormal production of histamine in the tissues, but they do prevent it from producing its customary effects. If the effect of the drug on the tissues is removed then they will react in a normal manner to the influence of histamine. Two important practical applications result from this knowledge: (1) the action of the drug lasts only as long as its concentration in the tissues is sufficiently high, and, since the effect of a single dose lasts from five to eight hours, it is apparent that it must be administered at least three times a day and in some individuals five times a day; (2) the underlying allergic or anaphylactic tendency persists in spite of the drug, and therefore its administration has to be continued either indefinitely or at least until the allergic or anaphylactic tendency has spontaneously subsided, or until specific desensitization has been achieved. It is important to realize that the use of these drugs in no way absolves one from the responsibility of specific treatment if that be possible.

### DOSAGE AND METHOD OF ADMINISTRATION

Benadryl (P. D. & Co.) and Pyribenzamine (Ciba) are usually prescribed in 50-100 mg. doses. With neoantergan (Anthisan: M. & B.) the dose is 100-200 mg. The maximum daily dose of Benadryl is 400 mg., Pyribenzamine, 600 mg., and Anthisan, 800 mg. Antistin (Ciba), which has been recently introduced, would appear to have a similar action to Benadryl. Children tolerate antihistamine drugs very well. Between the ages of 2 and 5, 10-50 mg. of Benadryl or Pyribenzamine may be given in the day or up to 100 mg. of Anthisan. Between 5 and 12, 150 mg. of Benadryl or Pyribenzamine or 300 mg. of Anthisan may be given daily. Children over 12 can be given the same dose as adults. It is important that the doses given should be given at six to eight hour intervals during the day and the last one administered late in the evening to "cover" the night period.

The drugs are generally given by mouth. Parenteral administration is unnecessary and inadvisable. As these drugs have an unpleasant taste and are powerful local anaesthetics, the tablets should be swallowed whole and not chewed. Should they come in contact with the mucosa of the mouth or throat they may produce an anaesthetic effect which will last several hours. They may cause nausea and vomiting if given on an empty stomach, and should therefore be taken immediately after a meal. There is no contra-indication to giving ephedrine or adrenaline during their administration. Atropine preparations, however, are contra-indicated, particularly with Benadryl, which has itself an atropine-like action. Care has to be taken in the coincident administration of sedatives, as in many patients antihistamine drugs produce a profound soporific effect.

### TOXIC OR SIDE EFFECTS

The administration of a single dose of 100 mg. of Benadryl will result in unpleasant reactions in 60 per cent. of cases. Side-effects occur in 30 per cent. of cases treated with Anthisan and Pyribenzamine and are usually less pronounced than with Benadryl. Sleepiness is the principal reaction with all three drugs. Thus, the practical superiority of Anthisan and Pyribenzamine over Benadryl lies in the fact that they can be tolerated in larger dosage and so may benefit some patients in whom the necessarily smaller dose of Benadryl had proved ineffective. Further, the stronger atropine-like action of Benadryl leads frequently to an unpleasant dryness of the mouth. Other common side-effects of these drugs are a feeling of fatigue, headache, nausea, dizziness, an unpleasant sensation of nervousness and tension, and occasionally vomiting and diarrhoea. In about 5 per cent. of cases these side effects are so distressing as to necessitate discontinuing the particular preparation responsible. Under these circumstances one of the alternative drugs should be tried before the use of antihistamine drugs is abandoned.

There are two methods whereby drowsiness may be minimized. One is by giving small doses initially and then gradually increasing the quantity till at the end of two or three days the full therapeutic dose is reached; in this way the patient becomes habituated to the drug, and the tendency to sleepiness usually wears off. Alternatively amphetamine may be given. A dose of 5 mg. in the morning will minimize the drowsy feeling. After a few days the administration of amphetamine can be stopped in the majority

of cases. The administration of amphetamine is contraindicated if the patient becomes nervous and apprehensive when taking the antihistamine. As mentioned above, any tendency to nausea may be minimized by never taking the drug on an empty stomach.

No deaths or toxic effects leading to organic change have been reported. Patients have now been taking antihistamine drugs continually in full dosage for over two years without ill effect, and increased tolerance does not seem to occur. In some cases it has been possible to reduce the dose gradually over a period and still maintain control of the allergic state.

### INDICATIONS FOR TREATMENT

**Urticaria and Angioneurotic Oedema.**—Over 80 per cent. of cases will be dramatically controlled with any of the three drugs mentioned above. The first obvious therapeutic effect is diminution of the skin irritation, and this occurs in half to three hours after the first dose has been taken. This is followed by a decrease of the number of lesions appearing. The daily dose should be gradually increased till full control is established. The importance of giving regular well-spaced dosage during the day so as to maintain an adequate concentration of the drug in the tissues should again be stressed. A number of cases will respond to Anthisan and Pyribenzamine and not to Benadryl, due either to the fact that larger doses of these preparations can be tolerated or that they are more effective antihistamines. Occasionally Benadryl will produce better results—usually in cases where the additional sedative effect of the drug is of advantage. As one would expect from the mode of action of antihistamines, very little effect will be produced on established lesions which will subside spontaneously, though they will prevent new lesions from occurring. Thus, in cases where there is swelling of the tongue or oedema of the glottis, adrenaline should be given in addition.

**Asthma.**—Sufficient time has not yet elapsed to enable a final opinion to be given as to the value of these drugs in asthma, though the writer's experience with them in this disorder has been extremely disappointing. This is hardly surprising, as the ætiological factors in asthma are usually multiple and much more complex than a simple histamine shock. It is probable that antihistamines do not have any beneficial effect in more than one patient in five, though it has been claimed that Pyribenzamine produces improvement in 40 per cent. of cases. The patients in whom beneficial effects are most likely to be produced are those with other obvious allergic manifestations such as eczema, vasomotor rhinitis, hay fever and urticaria, and its use should be reserved for such cases. The drugs are valueless in the treatment of the acute asthmatic attack.

**Hay Fever and Perennial Vasomotor Rhinitis.**—Complete relief of nasal irritation, sneezing and rhinorrhoea results from administration of these drugs to patients suffering from hay fever in at least half the cases. In a further 25 per cent., though complete amelioration of symptoms does not occur, sufficient symptomatic improvement takes place to justify their use. In about 25 per cent. of cases there is no improvement and occasionally the condition seems to be aggravated.

In perennial vasomotor rhinitis results are less promising, but a sufficient number are improved to justify a trial of antihistamine therapy. Benadryl,

however, has proved disappointing and Pyribenzamine and Anthisan are the drugs of choice. When large polypi or gross infection are found to be present in the nose, these conditions should be treated before resorting to the use of antihistamines.

**Drug Sensitivity.—Liver.**—In patients manifesting mild reactions to parenteral liver therapy a single dose of 300 mg. of Anthisan has been shown either to control completely, or diminish markedly, the reaction. In a moderately severe case one gramme of the drug in divided dosage is given over a period of 24 hours, followed by a further single dose of 300 mg. administered one hour before the injection of liver extract. This will control the majority of symptoms and enable the continuation of liver therapy until such time as desensitization (see p. 482) can be carried out. In a very severe case antihistamine drugs will only modify the reaction. In such patients it has also been found that even after desensitization a single dose of an antihistamine drug may still be required before each injection of liver extract.

**Insulin.**—This usually manifests itself as an annoying local reaction which passes off in a few days. Occasionally, however, a generalized urticarial reaction occurs which may be alarmingly severe for a day or two. The administration of antihistamine drugs is of value in these cases. They only require to be given for a period of a week or so when spontaneous desensitization may be confidently anticipated.

**Penicillin and Sulphonamides.**—Urticarial reactions to these drugs—particularly penicillin—are quite common, and complete control or modification of the urticaria results from the administration of antihistamine substances in the great majority of cases. Much more rarely penicillin may cause a reaction of the serum sickness type. The joint pains associated with such a reaction are usually little influenced by antihistamines though the other manifestations of serum sickness may be so much improved as to allow specific therapy to be continued. Serum sickness due to other causes is also benefited (see p. 66).

**Anaphylaxis.**—(See p. 69.) Antihistamine drugs will *not* control the manifestations of anaphylaxis, but they will moderate the severity of the reaction. There should, however, be no relaxation of the usual precautions (see p. 69).

**Intractable Skin Irritation.**—The distressing pruritus of dermatitis, pruritus vulvæ and ani, and the pruritus of drug rashes and jaundice are usually considerably alleviated by these drugs, so that the patient ceases to scratch, with resulting improvement. The writer's limited experience suggests that Benadryl is perhaps more efficacious than Anthisan in the dermatoses as the stronger sedative effect of the drug is probably of advantage in such conditions.

There is insufficient evidence at present to be able to assess the value of antihistamine drugs in other presumed allergic states such as migraine, purpura, gastrointestinal allergy and per-arteritis nodosa.

R. B. HUNTER.

# DEHYDRATION AND HYPOCHLORAEMIA

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**D**ISTURBANCE of the interchange of water and salt between the body and its environment through deficient intake or excessive loss from the body of either water or salt or both leads to a reduction in the amount of water in the body. The resulting syndromes are therefore grouped under the general term "dehydration," but the mechanism whereby dehydration is produced, the resulting clinical manifestations and the appropriate treatment differ radically according to whether the dehydration has been occasioned by loss of water or of salt. An understanding of the mechanisms leading to dehydration is therefore essential if correct treatment is to be given. This has been the subject of an excellent review by Marriott in his recent Croonian lectures, of which liberal use has been made in the writing of this section.

## ANATOMY AND PHYSIOLOGY OF THE BODY FLUIDS

The body fluids can be considered as being divided into two main compartments—the extracellular and intracellular compartments. The extracellular compartment consists of two portions—the blood-plasma and the interstitial fluid (including lymph). Of these, the intracellular compartment is much the largest.

Besides differing in anatomical situation, the body fluids in the various compartments differ also in chemical composition. The blood-plasma and interstitial fluid are separated by the membrane of the capillary walls, which is permeable to all the constituents of the plasma except protein. Interstitial fluid is therefore essentially a protein-free filtrate of plasma, and in any adjustment of osmotic balance between the two, movement of both water and salts can take place between the compartments. The intracellular fluid is separated from the extracellular fluid by the membranes of the body cells, which are freely permeable to water but impermeable to the chief cations of the body fluids—sodium in the extracellular fluid and potassium in the intracellular fluid. Regulation of osmotic balance between the two fluids can therefore only take place by a shift of water in one or other direction across the cell membrane.

## THE WATER BALANCE OF THE BODY

Water is added to the body by the taking of fluid as such or from the water content of solid food, and by the liberation of water produced in the oxidation of foodstuffs within the body.

Loss of water from the body occurs through four channels:

(1) Insensible perspiration—the passive diffusion of water vapour from the lungs and through the skin. The quantity of water so lost amounts to 1,000 to 1,200 c.c. daily.

(2) Sweat—secreted as required for the dissipation of the body heat. Sodium chloride, averaging about 0.25 gm. per 100 c.c., is lost in the sweat.

(3) The intestines—except in diarrhoea, only a little water, about 100 to 200 c.c. daily, is lost in the fæces.

(4) The urine. From the point of view of water balance, urinary secretion can be divided into:

(a) obligatory urine secretion—the amount of urine required to rid the body of soluble waste products at the maximum concentrating power of the kidneys. The amount of obligatory urine therefore varies with the quantity of waste products and with the concentrating power of the kidneys; in a healthy adult it is in the region of 500 c.c. per day;

(b) excretion of the excess of water that is not got rid of by the other channels.

The minimum water intake will therefore be the amount that satisfies the losses through insensible perspiration, obligatory urine and any active sweat secretion. The two former make up about 1,500 c.c., while the latter ranges from negligible amounts in temperate climates to 10 to 12 litres daily under tropical conditions.

The constancy of body water in health is controlled by the kidneys, chiefly through hydrostatic and osmotic mechanisms, but also partly by the action of the antidiuretic hormone of the posterior pituitary gland in promoting the reabsorption of water in the renal tubules.

### THE SALT BALANCE OF THE BODY

The body is entirely dependent on the food for its inorganic bases, including sodium, whereas much of the acid is formed in metabolism. The salt balance of the body therefore hinges largely on the conservation of inorganic bases.

The body can conserve sodium and other inorganic bases much more efficiently than it can water. Except in conditions causing profuse sweating, the main channel of salt excretion is in the urine. If salt intake is deficient and there is any tendency for the plasma sodium chloride concentration to fall below normal, excretion of salt by the kidneys practically ceases. The minimum salt intake to preserve salt balance is therefore very small—less than 1 to 2 gm. daily, so that the amount of salt normally ingested, about 10 gm. daily, is much in excess of the minimum requirements. It follows that salt depletion does not occur under conditions of reduced intake, but requires some abnormal loss—in sweat, alimentary secretions (vomiting or diarrhoea) or urine.

Like water, the constancy of the salt content of the body is maintained chiefly by the hydrostatic and osmotic mechanisms operating in the kidney, but it is also partly under hormonal control. Most of the salt that is not reabsorbed in the renal tubules by osmotic effects is reabsorbed under the influence of the adrenal cortical hormones, particularly desoxycorticosterone. In adrenal cortical deficiency there is a failure of reabsorption of a certain proportion of the sodium chloride of the glomerular filtrate and the kidneys lose the power of retaining sodium in the face of a fall of the sodium chloride concentration of the plasma to subnormal levels.

### THE PATHOGENESIS AND SYMPTOMATOLOGY OF DEHYDRATION

A very important advance in our understanding of the mechanisms underlying the dehydration so often encountered in seriously ill patients has been the experimental demonstration that there are two distinct types of dehydration, one due to a shortage of water alone and the other caused by a loss of salt in the presence of an unrestricted water intake. Both mechanisms may be operative under conditions of water shortage coupled with abnormal salt loss, so that a third or mixed type of dehydration must be considered.

**Water Depletion** (*Primary Dehydration*).—This occurs when the minimal water losses of the body, represented in temperate climates by the insensible perspiration and the obligatory urine secretion, are not met from ingested water or water formed in metabolism.

Such water depletion can and does occur in ordinary medical practice in circumstances where a patient is unable to drink, either because of some obstructive lesion in the mouth or œsophagus, or in coma or even great weakness, where the patient, although conscious, is too feeble to satisfy a thirst that may be dulled by the primary disease.

The water lost through lungs, skin and urine is drawn first from the extracellular fluid, which therefore tends to become hypertonic in relation to the cellular fluid. Since the cell membranes are impermeable to sodium and potassium ions, osmotic equilibrium can only be re-established by water being sucked out of the cells into the extracellular fluid, whose volume is therefore maintained to a great extent. Water depletion thus results chiefly in a loss of cellular fluid.

The earliest and one of the most prominent symptoms of water depletion is thirst and dryness of the mouth. Progressive weakness supervenes after three to four days, and later mental confusion and temperamental changes may develop, and the condition progresses to one of collapse.

The body-weight falls in proportion to the water deficit and the patient looks ill and pinched. The urine volume falls rapidly to the minimum necessary for the elimination of waste products (about 500 c.c. daily) and remains at this level as long as the blood pressure is high enough to ensure glomerular filtration.

Since the main weight of the water loss falls on the cellular fluid, plasma volume is little if at all reduced, and the hæmatocrit level, and hæmoglobin and plasma protein concentration remain deceptively normal. The plasma sodium chloride content tends to rise, but the main change in the blood chemistry is a slow but progressive rise in the blood urica, probably due to an increased breakdown of tissue protein resulting from cellular dehydration.

**Salt Depletion** (*Secondary Dehydration*).—Abnormal loss of salt is seen in uncomplicated form in profuse sweating where there is no limitation of water intake.

The commonest causes of abnormal loss of sodium chloride in temperate climates are vomiting and diarrhœa. If the patient's water losses are replaced by unsalted fluid, a state of pure salt depletion and secondary dehydration will develop in spite of an adequate fluid intake. Suction drainage of either gastric or intestinal contents carried out for therapeutic purposes can lead to equally great losses of salt.

Abnormal loss of salt in the urine is best exemplified by Addison's

disease, where, as we have seen, there is excessive salt excretion in the urine even when the plasma sodium chloride content has fallen below normal. But abnormal salt loss in the urine occurs in two more common diseases—diabetic acidosis, and the terminal uræmic stage of chronic nephritis. In diabetic acidosis there is an excessive loss of inorganic base in combination with the keto-acids; in uræmia, the ammonia-forming powers of the kidneys are reduced so that fixed base has to be used to neutralize the acid end-products of metabolism, and the kidney also loses the power of conserving salt in the face of a falling plasma sodium chloride concentration.

Loss of sodium from the extracellular fluids in salt depletion means that these would become hypotonic in relation to cellular fluid if no adjustment were made. To maintain osmotic equilibrium between extracellular and cellular fluids, an amount of water corresponding to the sodium lost is excreted by the kidneys, and the net result is therefore a localized dehydration involving the extracellular fluid, the volume of cellular fluid being unaffected.

The clinical manifestations of salt depletion are therefore largely those of peripheral circulatory failure, terminating in oligæmic "shock." Increasing lassitude and apathy, out of proportion to that expected from the primary disease, is probably the earliest symptom; this may be followed by mental confusion, progressing to stupor. There is well-marked muscular weakness, and muscle cramps are common, especially in muscles suddenly brought into action.

Gastro-intestinal symptoms, important not only in themselves but because they aggravate the salt depletion, are prominent. They include anorexia and nausea not noticeably related to food, and vomiting is common. The former symptoms lead to a curtailment of salt intake and the vomiting adds to its loss. It is therefore not surprising that rapid deterioration of the patient's condition sets in with the onset of these symptoms.

Signs of subcutaneous dehydration become obvious—slack, inelastic skin, pinched face with sunk cheeks and cyanotic lips, and reduced eyeball tension. The body-weight falls, but not as rapidly or to such an extent as in primary dehydration.

The pulse becomes small in volume and later quick and thready. The blood pressure is not reduced in the early stages, but falls later as circulatory failure becomes more severe.

There are two important negative findings that must not be allowed to interfere with early recognition of the salt depletion syndrome. Firstly, there is no thirst, although there may be a peculiar sensation in the mouth and a blunting of the sensation of taste. Secondly, if the patient is taking fluid freely, the urine volume is not decreased, owing to the efforts of the kidneys to maintain the osmotic pressure of the extracellular fluids by excreting any water in excess of the reduced amount balancing the depleted extracellular electrolyte content. In the final stage of oligæmic shock, however, anuria may supervene when the blood pressure falls below the level necessary to maintain glomerular filtration.

In contradistinction to water depletion, evidence of a reduction in plasma volume is apparent either by direct measurement or by the increasing hæmatocrit readings, red cell count, and hæmoglobin and plasma protein levels. The blood urea rises more rapidly and to higher levels than in water depletion, because some degree of renal failure is present as well as an



increased rate of tissue protein katabolism caused by the interference with the nutrition of the body cells that results from the reduced volume and increased viscosity of the blood. In spite of the efforts of the kidneys to maintain the electrolytic isotonicity of the extracellular fluid, the sodium and chloride content of the plasma is reduced if the salt depletion is severe. But because of the great reduction in the volume of extracellular fluid, the fall in the plasma levels of sodium and chloride does not give anything like an accurate index of the total deficit of these ions.

Except in Addison's disease and sometimes in uræmia, the kidneys cease to excrete sodium chloride when the plasma levels of sodium and chloride tend to fall below normal. Absence of chloride in the urine is therefore a much more reliable test of salt depletion than investigation of the plasma levels of sodium or chloride. This test can be carried out very simply in the clinic by the method of Fantus:—

All that is required is a small test-tube, a dropping pipette with a rubber teat, 20 per cent. potassium chromate solution, 2·9 per cent. silver nitrate solution and some distilled water. Ten drops of urine are measured into the test-tube, the pipette is rinsed with distilled water, and one drop of potassium chromate solution added to the urine as the indicator. The pipette is rinsed with distilled water again and silver nitrate added drop by drop with shaking until there is a sharp colour change from yellow to brown. The number of drops of silver nitrate required to produce this colour change gives a measure of the chloride content of the urine in grams of sodium chloride per litre. (*N.B.*—The reagents should always be examined for freedom from chloride by a preliminary test with distilled water in place of urine.) A virtual absence of chloride from the urine, as indicated by the colour change on the addition of only one drop of silver nitrate, means that salt depletion is present, although in Addison's disease and uræmia, as we have seen, sodium chloride will still be present in the urine even in the presence of salt depletion.

**Mixed Water and Salt Depletion.**—This will occur in patients suffering from abnormal losses of salt in secretions in whom there is also a restriction of the fluid intake. Water loss will tend to outstrip salt loss owing to the continued unavoidable water loss through lungs, skin and urine. Severe vomiting where the patient is unable to retain even water by mouth is the commonest cause of this mixed type of dehydration.

The clinical manifestations of mixed water and salt depletion are naturally a combination of the salient features of the two pure types of dehydration. Patients will suffer from the peripheral circulatory failure of salt depletion, but there will also be thirst, dry mouth and oliguria.

## TREATMENT OF DEHYDRATION

### PROPHYLAXIS

It should not be an unrealizable ideal that in every seriously ill patient the medical attendant should satisfy himself that enough water and salt is being ingested to cover the losses of both from the body. This is especially necessary in cases suffering from abnormal losses of bodily secretions.

Precise figures cannot be given for the desirable intakes of water and salt, for these will vary with the nature of the disease under treatment. The minimum water intake necessary to cover the various obligatory water

losses is about 1.5 litres daily in health, but obviously may be much greater in diseases associated with severe sweating or abnormal loss of alimentary secretions. The best guide to the adequacy of the water intake is the amount of urine secreted. This must cover the obligatory urinary secretion, and to give a margin of safety it is recommended that the volume of urine should not be allowed to fall below 1 litre ( $1\frac{3}{4}$  pints) daily; in cases where there is any reason to suspect renal insufficiency, either temporary or permanent, the desirable daily urine volume should be about  $1\frac{1}{2}$  litres (approx.  $2\frac{1}{2}$  pints). The specific gravity of the twenty-four hour urine should not exceed 1.020 if the water intake is adequate.

The minimum salt intake required to maintain metabolic balance is very small in health, being less than 1 to 2 gm. daily. Except in cases of congestive heart failure or of nephritis with oedema, it is unwise and undesirable to restrict patients to such a small salt intake, and at least 5 gm. ( $\frac{1}{8}$  oz.) of salt should be given daily, and more of course in cases with abnormal losses of salt. Where a fluid diet is being given, the salt may be included in broth or tomato juice, or beverages such as fruit cordials or tea can be made with 0.2 per cent. saline instead of plain water. The most certain method of ensuring that a patient is receiving a sufficient salt intake is by estimation of the sodium chloride concentration of the urine by the method of Fantus, described above; in adults this concentration should be 3 to 5 gm. per litre.

Wherever possible, the requisite amounts of water and salt should be taken by mouth. When the patient's condition precludes this, water and salt must be given as a continuous drip either by gavage (*i.e.*, through a tube introduced into the stomach via the mouth or nose), rectal infusion or parenterally by the intravenous route. In gavage, hypotonic fluids can be given, but in rectal or parenteral infusions the fluid should be isotonic. Isotonic or normal saline contains 8.5 gm. of salt per litre; the fluid requirement of 3 litres or upwards daily therefore must not be supplied exclusively as normal saline to a patient who is not suffering from salt depletion, since this would entail an excessive salt intake. Not more than one litre should be given as normal saline, and the remainder of the fluid intake given in the form of 5 per cent. glucose solution.

### TREATMENT OF ESTABLISHED DEHYDRATION

From what has been said regarding the mechanisms leading to the two types of dehydration from depletion of water and salt respectively, it is clear that the treatment required for each type is radically different. It must be emphasized, too, that wrong treatment may not only fail to relieve the dehydration but may even aggravate the patient's condition. Thus in pure water depletion there is no deficiency of salt in the body, and the patient needs water, and water only. If, instead of water, he is given saline, some of the water of this saline will be excreted in the insensible perspiration from the skin and lungs. This will leave an excess of salt in the body to be excreted by the kidneys, so that the volume of the obligatory urine secretion will be increased and the dehydration thereby aggravated. On the other hand, the administration of saline-free fluids to a patient suffering from pure salt depletion does nothing to relieve the secondary dehydration, for the absorbed water is excreted by the kidneys to maintain the osmotic

isotonicity of the extracellular fluids. If the peripheral circulatory failure has progressed to such a stage that the blood pressure is too low to maintain glomerular filtration and anuria has supervened, then the administration of salt-free fluid is actually dangerous. The kidneys can no longer maintain the osmotic isotonicity of the extracellular fluid by excreting absorbed water, and any water entering the blood stream and so rendering it hypotonic must pass into the body cells, producing the dangerous condition of water intoxication.

The first essential in the treatment of dehydration is therefore the accurate diagnosis of the type of dehydration present. The main features of water and salt depletion, and the mixed type of dehydration have been discussed, and only a brief recapitulation of the differential features need be made. The diagnosis will depend on :—

- (1) The history of the case with regard to manifestations likely to have led to depletion of water or salt or both.
- (2) The thirst and dryness of the mouth in water depletion and the absence of thirst in salt depletion.
- (3) The relatively fixed oliguria of water depletion as contrasted with the normal urine volume of the salt-depleted patient on an unrestricted water intake.
- (4) The normal or high chloride concentration in the urine in water depletion as contrasted with the minimal or absent chloride excretion in the urine in salt depletion (with the exception of Addison's disease and uræmia).
- (5) The absence of evidence of diminished plasma volume in water depletion as contrasted with the progressive hæmo-concentration (increased hæmatocrit reading, and increased hæmoglobin and plasma protein concentrations) in salt depletion.
- (6) The recognition that a combination of manifestations of hæmo-concentration and peripheral circulatory failure with thirst and oliguria points to the mixed type of dehydration caused by depletion of both water and salt.

In all three forms of dehydration the essentials of practical treatment are summed up in the answers to three questions : (1) What fluid should be given? (2) How much fluid should be given? (3) By what route and at what rate should the fluid be administered?

**Treatment of Water Depletion.**—The fluid to administer is obviously water, and if the patient is able to drink, water should be administered by mouth. If the patient is unable to swallow, water can be given by gavage or per rectum or isotonic (5 per cent.) glucose solution can be administered intravenously.

The aim of treatment is to restore the volume of cellular fluid and therefore the body-weight to normal as rapidly as is compatible with safety. The extent of the water deficit and therefore an indication of the amount of water required can be estimated roughly by considering the clinical condition of the patient in relation to three grades of severity:—

*Mild.*—Definite thirst, but no other manifestations of water depletion. Water deficit about 2 per cent. of the body-weight (i.e., about 1·5 litres or 3 pints in the "average" adult man of 70 kilograms or 11 stones).

*Moderately Severe.*—All the manifestations of water depletion present, but not to such a degree as to cause marked prostration or mental confusion.

Water deficit about 6 per cent. of the body-weight (over 4 litres or about 7 pints in the average man).

*Very Severe.*—All the manifestations of water depletion, including mental confusion and severe physical prostration. Water deficit of 7 to 14 per cent. of the body-weight (5 to 10 litres, or 9 to 18 pints in the average man).

The rate of administration will depend on the state of the patient. It must be remembered that the patient is continuing to lose water through lungs, skin and urine at the rate of at least 1.5 litres per 24 hours, and therefore in assessing the amount of fluid to be administered, this volume must be added to the amount considered necessary to make good the fluid deficit. This means that even the mildest case of water depletion will need at least 3 litres (about 5 pints) in the course of the first 24 hours. Where intravenous drip infusion of isotonic glucose has to be used to restore the depleted body water, this amount of fluid will necessitate a rate of flow of about 50 drops per minute. Where the water depletion is at all severe, the initial rate of flow should be increased to about 100 drops per minute for the first few hours and reduced later to 50 drops as the patient's condition improves. Pure water depletion does not demand such heroic measures of rapid intravenous infusion as are required in the peripheral circulatory failure of severe salt depletion, and restoration of the water deficit in a severe case can be allowed to occupy more than the first 24 hours. The best objective check on the efficacy of treatment in water depletion is the measurement of urine volume, and the aim should be the restoration of the amount of urine secreted to a volume of about one pint (570 c.c.) every eight hours.

**Treatment of Salt Depletion.**—The aim being to restore the volume of extracellular fluid as rapidly as possible, the fluid to use initially is isotonic saline.

The extent of the reduction in the volume of extracellular fluid can be gauged from estimations of plasma volume, either directly or by the formula proposed by Black, *viz.*, Plasma loss in litres =  $5 - \frac{500}{\text{Hb.}}$ , where Hb. represents

the patient's hæmoglobin percentage. To obtain the total loss of extracellular fluid, the plasma loss should be multiplied by 6.

A rough guide to the extent of extracellular fluid loss can be obtained by assessing the patient's condition in relation to three degrees of severity of salt depletion:—

*Mild.*—Minimal concentration or absence of chloride in the urine. Symptoms confined to lassitude and perhaps faintness on sudden assumption of erect posture. Salt deficit up to 0.5 gm. per kilo of body-weight, representing 4 litres (7 pints) of isotonic saline in an average man of 70 kilograms (11 stones).

*Moderately Severe.*—Absent urinary chlorides. Symptoms include anorexia, and perhaps nausea and vomiting, as well as lassitude and faintness. Blood pressure reduced, but systolic pressure above 90. Salt deficit 0.5 to 0.75 gm. per kilo body-weight, equivalent to 4 to 6 litres (7 to 11 pints) of isotonic saline in the average man.

*Very Severe.*—Absent urinary chlorides. Apathy, stupor, vomiting. Blood pressure reduced, with systolic pressure below 90. Salt deficit 0.75 to 1.25 gm. per kilo body-weight, representing 6 to 10 litres (11 to 18 pints) of isotonic saline in the average man.

Patients cannot be asked to drink the amounts of isotonic saline necessary

to restore even a mild salt depletion and the rectal route of infusion is too slow. Therefore a continuous drip must be given either by gavage (trans-nasal intragastric drip) or by the intravenous route; the latter is the method of choice in all but the mildest degrees of salt depletion.

As in water depletion, the rate of administration of fluid will be that which restores the patient's condition to normal as rapidly as possible consistent with safety. In the milder degrees of salt depletion it will be enough to give the normal saline at the rate of 100 drops per minute for the first hour or two, and then at a slower rate of about 50 drops per minute. This will suffice to restore the salt deficit within the first 24 hours of treatment. But where the salt deficit is more profound and the patient is showing evidence of peripheral circulatory failure, more heroic measures are necessary, and the rate of administration should be four pints in the first hour and a half of treatment, and thereafter a pint every two hours until the patient's blood pressure is restored to normal, and a pint every four hours after that until restoration of the body's salt content is indicated by a satisfactory excretion of sodium chloride in the urine. Serial tests by the method of Fantus of all samples of urine passed is therefore an essential check on the efficacy of treatment, and administration of normal saline should be continued until the patient's symptoms are relieved and chloride has reappeared in the urine; a careful watch must also be kept for signs of oedema, especially pulmonary oedema—evidence that excess of saline has been administered. At this point the giving of normal saline should cease, both to avoid the development of oedema and because there may be a tendency for patients to retain sodium and chlorine out of proportion to water. Half-normal (0.425 per cent.) saline must now be given, either by mouth if the patient can now drink or by the intravenous route by mixing equal volumes of normal saline and 5 per cent. glucose, until the salt deficit is made good, as shown by the passage of at least a pint of urine every eight hours containing 3 to 5 gm. of sodium chloride per litre. If the patient is now able to take food as well as fluid by mouth, the salt content of the former can be relied upon to provide enough for maintenance. Otherwise, administration of one-third normal saline (*i.e.*, one volume of normal saline in two volumes of 5 per cent. glucose solution) must be continued in amounts of about 3 litres (about 5 pints) daily.

**Treatment of Mixed Water and Salt Depletion.**—Where the need is for both water and salt, it is best not to give normal saline, even initially, since the introduction of an electrolytically isotonic fluid into the blood stream will not allow water to pass from the extracellular fluids to the cells. The kidneys rarely excrete chloride in a concentration as high as that of normal saline, so that they cannot get rid of more salt than water from the infused saline and so provide a surplus of water for restoration of the volume of cellular fluid.

The mixed type of dehydration should therefore be treated from the outset with half-normal saline, which can later be reduced to one-third normal when the urine volume approaches the desired level and chloride reappears in the urine, as described under salt depletion above.

#### TREATMENT OF DEHYDRATION IN INFANTS AND YOUNG CHILDREN

This subject demands special consideration, not only because of the frequency of diseases leading to dehydration at this age, but because of important physiological differences between the water and salt metabolism of infants and that of adults.

(1) During the first year of life the kidneys are relatively inefficient organs of excretion as compared with those of an adult. The urea and mineral clearances are lower per unit of surface area, which means that a less concentrated and therefore a relatively larger volume of urine must be excreted to get rid of waste products.

(2) The metabolism of infants and young children is relatively greater than that of adults. This leads to the formation of a proportionately greater amount of waste products requiring excretion.

These two factors together serve to make the volume of obligatory urine secretion, and therefore the unavoidable water loss, relatively much greater in an infant than in an adult. This explains why infants withstand water deprivation so badly, for their stores of body water are depleted much more rapidly than those of adults.

It is therefore of vital importance that an infant's urine volume must not be allowed to fall when water and salt are being lost, as in vomiting and diarrhoea. Although the alimentary secretions are isotonic with the body fluids, normal saline should never be used to replace water and salt loss in an infant unless he is taking water freely by mouth as well; water, but not salt, is being lost from the lungs and skin, and, as we have seen, the infant's kidneys are relatively inefficient in excreting any excess of salt that may be given.

The best procedure is to give an intravenous infusion of half-normal saline (*i.e.*, equal volumes of normal saline and 5 per cent. glucose) at once to an infant suffering from dehydration. The amount given will, of course, depend on the degree of dehydration, but a rough guide is a volume equivalent to 3 per cent. of the body-weight in mild cases and up to 6 per cent. of the body-weight in severe cases. This should be followed by a maintenance infusion of one-fifth normal saline (one volume of normal saline to four of 5 per cent. glucose solution) in amounts sufficient to meet the normal daily requirement of 2 to 2½ oz. of fluid per lb. of body-weight, or in the greater amounts needed to maintain body-weight if abnormal losses of fluid continue. The intravenous route using the drip technique is the most suitable, for it is the one by which the depleted body fluids can be restored most quickly.

Rectal infusion is suitable only in cases with vomiting but no diarrhoea. The subcutaneous route is only to be used as a supplement to oral administration of fluids since normal saline is the only suitable fluid—glucose solutions should not be used owing to the danger of abscess formation.

It is less easy to assess the progress under treatment than in an adult, owing to the difficulty of measuring urinary output. Daily weighing of the patient is helpful and is much more informative as to the state of the water balance than investigation of the blood chemistry. If urine is obtained, estimation of the chloride content should be carried out on each sample until chloride excretion is satisfactory. In this connection it must be remembered that, owing to the lower concentrating power of the infant's kidneys, the desirable chloride content of the urine will be less than in the case of an adult, a figure of 2 to 3 gm. per litre being sufficient.

I. A. ANDERSON.

# TUBERCULOSIS

## THE PREVENTION OF TUBERCULOSIS

**CAUSES of Decline in Tuberculosis Mortality.**—In the majority of Western European Countries and in North America the mortality from tuberculosis had been declining for many years prior to the recent war. In England and Scotland, for example, it had fallen during the fifty pre-war years by about 75 per cent. Moderately reliable tuberculosis mortality statistics became available coincidentally with Koch's discovery of the tubercle bacillus, which discovery set on foot the organized campaign against the disease. The decline in mortality thus became apparent at much the same time as anti-tuberculosis measures were initiated, and since then the fall in the one has run parallel with the development of the other. It was natural, therefore, for many to ascribe this gratifying decline entirely to the campaign which has been waged against tuberculosis. There is evidence to suggest, however, that the mortality from tuberculosis had been declining for many years prior to the special measures taken to combat the disease. It has been suggested that we are at present at the end of a protracted epidemic of tuberculosis, and that the disease is subject to the same epidemic waves as measles, scarlet fever and diphtheria, with this difference, that whereas the epidemic waves of these more acute diseases are relatively short, that of tuberculosis may last a hundred years or more. This is not beyond expectation in a disease which may continue during the lifetime of an individual, in contrast to epidemic diseases of a more ephemeral type. Further, it is probable that during such an epidemic communities which have been exposed particularly to the infection have acquired a strong resistance, and that those individuals who are peculiarly susceptible to infection have died at an early age, leaving relatively few descendants to inherit their peculiar susceptibility. Perhaps, too, the number of young people alive to-day is relatively less in proportion to the number of people over forty than was the case in the Victorian age, and it is well known that tuberculous disease, particularly in females, reaches its climax between the ages of twenty and thirty. Thus the fall in the mortality from tuberculosis may be the outcome of a progressive decline of an epidemic wave in a community whose resistance is progressively increasing.

Whether or not we believe that these are pertinent factors in producing the fall in the mortality from tuberculosis, it should not lead to a fatalistic outlook towards the preventive aspects of the disease. There is no reason to believe that an epidemiological cycle cannot be modified beneficially by human efforts. No one, for example, would suggest that the worst effects of epidemics of acute infectious diseases cannot be reduced by popular education, by social and public health measures and by the private efforts of medical practitioners. The same can be said of tuberculosis. Acknowledgment that we may be unable to assume that the *entire* fall in the mortality from tuberculosis has been due to anti-tuberculosis measures does not justify the opposite attitude not infrequently adopted. It is unjusti-

fiable to make light of the great efforts which have been made to combat the disease, or to deny that these have been a potent contributory factor in lowering the mortality from tuberculosis. We need only look, for example, to the increase in tuberculosis in countries ravaged by war, to its disproportionate incidence in certain trades, to its wide occurrence in districts smitten by poverty and unemployment and to the rarity of glandular and bone and joint tuberculosis in countries with a clean milk supply, to be certain that epidemiology, immunity and natural selection are not the sole factors in the distribution of tuberculosis.

**Infection.**—The factors contributing to the extension of tuberculosis are many, but the essential cause is contagion from a human or animal source. It is therefore of interest to inquire to what extent infection can be avoided, and whether attempts to prevent infection should occupy an important place in anti-tuberculosis measures, and if so, in what direction. The answer depends on whether adult exogenous infection occurs with significant frequency in civilized communities. Opinions differ widely on this matter, but it is an important one for the practitioner whose opinion may be sought by patients as to whether they are likely to infect their husbands, wives or adult friends, and by employers as to the danger to others of a tuberculous employee in their premises. We believe that adult tuberculosis usually occurs as a late manifestation of an earlier infection, just as general paralysis is a late manifestation of syphilis, and that it is uncommon for an *adult* to develop tuberculous disease as the result of an outside superinfection, provided he is already protected by an earlier inoculation. It should be remembered that in older children and adults a positive tuberculin reaction is a desirable rather than an undesirable acquisition. When tuberculous disease does occur in an adult it is usually due to the breakdown of an already established infection and not to a new one.

Not infrequently a high rate of tuberculous morbidity is witnessed among medical students and nurses as the result of contact with cases of open tuberculosis. This excessive morbidity, however, chiefly occurs among those probationers and students who exhibit a negative tuberculin test on starting training, and who accordingly do not have the increased resistance given by a previous infection which has been successfully overcome. All nurses and young adults about to be brought into close and continuous contact with cases of open tuberculosis should be tested with tuberculin, and those who are negative reactors should, if at all possible, be prevented from taking such a considerable risk.

Immunity in tuberculized adults to exogenous reinfection may disappear, just as it may in the common exanthemata. At best it is not absolute. It modifies rather than prevents reinfection and can be nullified by anything which greatly lowers the resistance of the individual, or by very massive doses of infecting bacilli. A doctor cannot, therefore, *guarantee* that a tuberculized adult will not be reinfected, just as he cannot *guarantee* that an individual will not take measles twice, but he can say that the risk is relatively slight. No doubt, also, this adult immunity may be temporarily in abeyance as the result of one of the acute infectious fevers like measles, or during the puerperium, when a massive exogenous infection may cause tuberculous disease. Care should therefore be taken at such times that the patient is not nursed by, or brought into close contact with, cases of open tuberculosis.



In the majority of cases it is difficult to reinfect a previously tuberculized adult just as Koch found it difficult to reinfect a tuberculous guinea-pig, and statistical evidence of the relatively low incidence of disease in the marriage partners of tuberculous adults is in keeping with this fact. The incidence of marital tuberculosis is, however, higher than in similar age-groups of the population. That reinfection from outside sources, although perhaps rare, can take place is an established pathological fact, and unnecessary risks, particularly with children and young people, even when they are known to have been already tuberculized, should be avoided. Our aim should be to avoid exposure to infection. This is particularly necessary in infancy when the mortality is very high, but it applies equally to childhood and the years of adolescence. It is during the latter period that the mortality curve from pulmonary tuberculosis rises sharply and the disease takes a heavy toll of young adults. There is evidence that many of these young people fail to resist a primary infection received at this comparatively late but susceptible developmental period, and the anomaly arises of the postponement of infection by improved hygienic and social measures to a later and in some ways even more dangerous period. This postponement of the age of infection has been in progress for many years and the persisting high mortality in young adult life is a disturbing fact. It raises preventive problems of great importance.

There is no doubt that the infection of tuberculosis must be avoided whether it be from the milk of tuberculous cattle or from contact with infectious consumptives. That tuberculous infection can be avoided for a lifetime is unlikely—we know that from tuberculin survey statistics—and the possibility of protection at the susceptible periods of infancy, childhood and young adult life must be considered.

The increase of tuberculosis during the recent war has thrown a heavy strain upon sanatorium beds which have been reduced in number by difficulties of securing nursing and domestic staff. It is at any time difficult to isolate the adult consumptive and it is impossible to isolate him permanently. It is equally difficult to remove the child or young adult from his infectious home surroundings, and a preventive impasse is reached. Under these circumstances the young contacts must be watched carefully for symptoms suggestive of tuberculous disease and they should be X-rayed, if possible, every six months. That will in all probability be done by the Tuberculosis Service of the Local Authority. There is, however, a great deal which the doctor can do himself. If it is impossible to remove the young contact to the home of a relative, every effort should be made to keep contact in the home as remote as possible. In certain overcrowded houses this may present almost insuperable difficulties, and it is unfortunately not uncommon to find a tuberculous subject not only sleeping in the same room but even in the same bed as a young child. This is, of course, an administrative and social scandal, and disaster under such circumstances is almost inevitable. In cases in which it is impossible to avoid having an open case of tuberculosis and a young child in the same house, it should usually be possible to arrange for the patient to have a separate sleeping room from which the child should be excluded, and to have separate utensils for eating and drinking and separate towels and bedclothes. All sputum should be ejected into a flask or paper handkerchief, which latter should be promptly burnt. Further, the patient should, as far as possible, avoid touching the child,

who should never be taken on his knee and never on any account kissed. It should always be remembered that contact with a tuberculous patient, or the conveying of infected material to the mouth, are probably almost as common causes of massive infection as "droplet infection," which receives such a prominent place in tuberculosis literature.

Statistics of family histories of young adults who develop pulmonary tuberculosis show that only about 40 per cent. have been in close contact with known cases of tuberculosis. Of the remaining 60 per cent. it is probable that an appreciable percentage develop pulmonary tuberculosis as the end-result of an infection received in earlier childhood, but there is conclusive evidence that the disease in many is the direct outcome of a recently acquired tuberculous infection. The problem is thus complicated. It includes those already discussed who are in known contact with infection, those known from a positive tuberculin test to have been already infected, and those known from a negative tuberculin test to have escaped infection. The heavy incidence of pulmonary tuberculosis in young adult life, irrespective of known contact infection, shows this to be a susceptible period. It is a time when the physiological stress of development is complicated by the strain imposed by altered conditions of work and travel which often accompany entry into employment or training, and deviations from health in these years should be investigated carefully with tuberculosis always in mind. To remember the possibility of tuberculosis often leads to its diagnosis.

B.C.G. vaccination has not been tried on any scale in this country and many of the original communications on its use were statistically valueless. There are now, however, well-documented records of its use in Scandinavia, America and Canada, and its efficacy as an immunizing agent is no longer in doubt. There is no such thing as permanent or complete immunity to tuberculosis, but B.C.G. does give an increased power of resistance to tuberculous infection which lasts for at least two years. The vaccine is harmless and it will probably be used in this country when centralized arrangements for its manufacture and control can be arranged. It must, however, be remembered that in tuberculosis any bacillary immunizing agent can only be effective in those who have not already been infected. The infected body will resist its entrance just as it resists that of a fresh tuberculous infection, and B.C.G. can only be used to protect against subsequent infection those who, as shown by the tuberculin test, have not already been infected. Its obvious use is in young people who fail to react to tuberculin, and that implies a scheme of universal tuberculin testing. There are two groups in which its use is essentially indicated—the newborn child in the tuberculous household and the young tuberculin-negative adolescent. The immunity which it can undoubtedly produce may in time play a part in reducing the heavy mortality at these age-periods.

If the segregation of the young child from massive human infection is a matter of extreme difficulty, its segregation from massive infection from milk is eminently practicable. There is no doubt that tuberculosis due to the bovine bacillus is responsible for a considerable percentage of tuberculous morbidity among children, particularly in Scotland. Though the bovine type of disease is mostly to be found in glandular, lupoid, abdominal, bone and joint and meningeal lesions, yet it may on occasion cause any type of tuberculosis—not even excluding the pulmonary variety. Having regard

to the great prevalence of tuberculosis among dairy herds in this country, and to the absence of a comprehensive national plan for dealing with it, it is clear that if conditions are allowed to remain as they are, large numbers of children are doomed to become victims of bovine tuberculosis. In several countries, notably America and New Zealand, bovine tuberculosis has been largely eradicated by ensuring a clean milk supply, but in this country large quantities of tuberculous milk are still consumed. It is common to hear the remark that a child is all the better for being immunized by a small dose of bovine bacilli. Unfortunately one cannot regulate the dose, and no one would be so bold as to suggest that it is good for a child to drink a teaspoonful of tuberculous pus in its milk.

Wherever possible "certified" or "tuberculin-tested" milk should be given to young children. Unfortunately it is often impossible to procure such milk, and even when procurable its expense makes it prohibitive to large sections of the community. Until, therefore, the ideal of a national clean milk supply is achieved, it is essential that all milk given to young children should be pasteurized. It is true that this method is not an absolutely complete safeguard in preventing the occasional occurrence of tubercle bacilli in milk, and that in the process certain quite insignificant losses occur in respect of its vitamin and mineral content. No one, however, can believe that these drawbacks are at all comparable to the great risks to which children are exposed by consuming unpasteurized milk from herds which have not been tuberculin tested. Even pasteurized milk is, however, often unprocurable, especially in rural districts. In such cases milk for young children should be boiled, or dried milk should be used.

Such measures to prevent bovine tuberculous infection are not so necessary in the case of older children and adults whose tuberculin reactions have already become positive. Clean milk is, however, *ideal* for them also, as tuberculosis is not the only disease conveyed through milk.

**Resistance.**—Having taken steps against the massive contamination of virgin soil by segregation and by the provision of a safe milk supply, other factors which predispose to infection must be looked for, not so much among the seed as in the soil in which the seed is sown. That is, infection is almost certain to take place—ideally in small and infrequent doses—and therefore all our efforts should be directed, not so much to the prevention of infection as to raising the resistance of the infected individual, particularly the young adult, against the infection becoming an established disease.

Apart from the question of race and breeding, over which we have no control, the resistance of an individual to his tuberculous infection will depend very largely on certain environmental conditions: housing, nutrition, habits and intercurrent infections.

One has only to reflect on the statistics forthcoming from all over the world to see that tuberculosis and overcrowding go hand in hand, though the relative importance of overcrowding will depend to some extent on collateral factors. Overcrowding is a factor which is capable of correction in the course of time, and the problem is still to the forefront. There is reason to believe that the better housing of the future will bring about a diminution in the incidence of the disease. Overcrowding is a national problem rather than one for the medical practitioner, though he may on occasion assist in procuring more suitable accommodation for the tuberculous families in his practice.

If, on the other hand, good environmental conditions as regards housing are only obtained at the expense of increased rents and travelling expenses, and therefore of a reduction of the family's food-purchasing power, the advantages which accrue from good housing may be considerably outweighed by nutritional deprivation. There is indeed definite statistical foundation for the statement that under-nourishment is the most important factor in predisposing an individual to tuberculous disease. Up till now the principles of good nutrition have been largely neglected in the medical curriculum. While every doctor can prescribe bottles of medicine, comparatively few can give sound advice as to how money can be expended most profitably on food. An educational campaign by doctors on the subject of nutrition, particularly among girls and housewives, would be more conducive to national physical fitness and the prevention of tuberculosis than any other form of public health propaganda.

**Early Diagnosis.**—It is apparent that preventive measures alone cannot be expected to be entirely successful without the early diagnosis of the disease. When a case of tuberculosis occurs in a household it is the family doctor's duty, in conjunction with the district tuberculosis officer, to search for a possible source of infection among the other members of the family. A child dying from tuberculous meningitis is frequently found to have a parent or grandparent supposed to be suffering from chronic bronchitis, but who is actually a victim of chronic pulmonary tuberculosis. Further, all the other children and young adults in such a family should be carefully examined with the help of X-rays to eliminate the possibility of early tuberculous disease, and any subsequent illness from which they may suffer must be regarded by the doctor in the light of the family history.

In the past overemphasis has been laid on gross physical signs in the chest in the diagnosis of tuberculosis, such as impairment of the percussion note and the presence of bronchial breathing and crepitations. These are frequently difficult to elicit or entirely absent in early pulmonary disease. On the other hand, too little importance is attached to the general signs of tuberculous toxæmia, common to all forms of the disease, which are often apparent to the patient's relatives and friends but overlooked by the doctor, obsessed by his hunt for physical signs in the lungs. Again, the significance of history-taking in the diagnosis of early tuberculosis is often insufficiently appreciated, and yet the majority of patients repeat with variations the same history with the regularity of a theme in a symphony. Early disease can usually only be *suspected* by the practitioner, and to clinch the diagnosis an appeal has often to be made to radiological and bacteriological examinations. These special services for the diagnosis of tuberculosis are available free of cost in all parts of this country and full use should be made of them. It may be that in the future the "mass" X-ray examination of young people entering the public services, large industrial concerns, or firms or professions in which employment may be pensionable will go far to solve the problem of early diagnosis, provided the X-rays are wisely interpreted.

Lastly, it should be remembered that other diseases, such as measles, whooping-cough, diabetes, silicosis and influenza, predispose towards tuberculosis. The prevention of such diseases and their correct treatment would assist indirectly in the prevention of tuberculosis, and suspicious symptoms occurring in the victims of such diseases should be given due regard.

## PULMONARY TUBERCULOSIS

### GENERAL MANAGEMENT

In the following pages the general management of a case of pulmonary tuberculosis will be described. Pulmonary tuberculosis is only one of the local manifestations of the disease, and the general treatment of pulmonary tuberculosis applies no less to other forms of the disease.

When a patient develops pulmonary tuberculosis there is often a natural disinclination on the part of the family doctor to reveal the true nature of the illness. Euphemisms such as "a spot on the lung" or "a slight inflammation of the lung" are often used. This is undoubtedly a mistake and often deludes the patient into a sense of false security, so that instead of putting himself immediately under strict treatment he compromises by going away for a holiday or by going to bed for a week or two. Valuable time in an early case is thereby lost. A patient is entitled to know the nature of his condition, even if the disclosure causes considerable temporary distress.

To a layman the title tuberculosis has a sinister significance. Patients think of it as an incurable and fatal disease, and feel that some sort of stigma is associated with it. It should be explained that tuberculosis, as we recognize it nowadays, is quite different from the "consumption" of the Victorian era. The disease was then seldom recognized till it had reached an incurable stage. Even if it was diagnosed relatively early, the correct method of treatment was unknown. The patient can be told that tuberculosis, far from being incurable, is a condition to which human beings are peculiarly resistant; that nearly all of us are infected by it, and that many of us without having been aware of the fact have indeed suffered from it slightly and have completely overcome it. Accordingly he must be made to realize that with wise management there is no reason at all why he should not make a complete recovery. Even moderately advanced cases should be encouraged in this way, for hope is a great therapeutic agent, and there are indeed few cases so severe when first seen that a hopeless prognosis can be given with any degree of certainty. At the same time the patient must be told that it is of the utmost importance for him to go under strict treatment at once, and that this will consist, among other things, in complete rest for an unspecified period. He will then almost certainly ask how long he will have to stop work. It is very unwise for the doctor to commit himself on this point, especially as he himself can only have a vague idea of the probable duration of the disease. Too often the patient is told that three months in a sanatorium will put him right. The patient makes his arrangements accordingly and may be seriously inconvenienced when it is found later that he will have to stay there for a considerably longer time. In addition, the physician in charge of the sanatorium may be put in a difficult position. On the other hand, it is often injudicious to depress the patient at the beginning of treatment by the statement that he may have to be off work for a year or more. It is wiser and more honest, therefore, to answer the patient's question by saying that it is quite impossible at the outset to say how long he will have to be under strict treatment, since this entirely depends upon how he responds to it. He will have to reckon its duration, however, in terms of many months and not in terms of weeks. A young person may be encouraged by the suggestion that it is worth while

spending some months in enforced inactivity to begin with in order to ensure his health for the rest of his life.

**Sanatorium Treatment.**—The majority of patients with active tuberculosis should be advised that the first stage of treatment is best carried out in a sanatorium. This advice does not apply to elderly patients suffering from chronic fibroid disease, whose management presents a special problem of its own (see p. 127), or to patients so ill that the prospect of procuring arrest of their disease is unlikely. Unless young children are present in the house it is wiser to treat such patients at home. For the average case of exudative tuberculosis in a young adult, however, a period of sanatorium treatment is invaluable. Quite apart from any active form of curative treatment, such as collapse therapy, the experience gained by the patient through the routine of sanatorium life is most useful in educating him in the implications of his disease and in methods for regulating his life in the future. Very few patients gain this knowledge if they are treated from the beginning in their own homes. It is often difficult to explain to a patient the benefits which he may expect to derive from going to a sanatorium. He is apt to say: "Surely if I have to do nothing except to lie in bed in the fresh air and to have good nourishing food, I can be cured at home just as well as in a sanatorium." The conditions at home are, of course, often quite unsuited for mental and physical rest. All the circumstances of home life remind the patient of the active life which he formerly led and which he has had to abandon. In this connection it must be remembered that mental rest is only secondary in importance to physical rest. The doctor should try to persuade the patient to divorce himself entirely from his previous associations, to place himself confidently and unreservedly in the hands of others and to accept the situation in a resigned and co-operative spirit. Once a patient has made up his mind to do this he usually settles down into the sanatorium routine. He then realizes, perhaps for the first time, how ill he is and what an effort it had been to carry on his ordinary life. It is only with returning health that he begins to wish for a resumption of his former pursuits.

Sanatorium treatment is available free of cost for all in this country. Many of these public institutions are admirably run, and the after-care by the tuberculosis authorities in conjunction with the family doctor is excellent. Unfortunately this is not invariably the case. In some districts there is a scarcity of sanatorium beds, involving tedious delay in admitting patients in urgent need of treatment, and causing premature discharge of others before their disease has had a chance of becoming quiescent. Some sanatoria are poorly managed and quite inadequately equipped and staffed.

The financial difficulties of a family deprived of its breadwinner will also have to receive the practitioner's consideration. In this respect the help of the Care Committee attached to the local tuberculosis dispensary should be solicited.

Another problem may often arise among those well able to afford a private nursing home for an acute illness but quite unable to face the expenses (seven to ten guineas a week) of a private sanatorium for six months or a year. If the local public sanatorium is a good one, such patients should be advised to go there for their treatment rather than to put themselves to unwarranted financial strain for the sake, perhaps, of a single room and the small additional comforts of a private sanatorium. Since the

salary of such patients may be temporarily suspended and their earning capacity considerably reduced in the future, it is very important for them to conserve their finances in every way possible.

**Climate.**—There is a prevailing impression among the well-to-do that tuberculosis spells institutional treatment abroad—particularly in Switzerland. This is a complete fallacy. Climate is of much less importance in the treatment of tuberculosis than the excellence of the physiological régime which is instituted, and there are several admirably run private sanatoria in this country. A patient may be cured of his disease in the centre of a large city just as well as in the middle of a pine forest or on the slopes of a Swiss mountain. It is scandalous how seriously ill patients are sometimes sent to die far away from their relatives and home comforts. That they should be subjected to the fatigue of a long journey and the indifferent nursing frequently encountered in a foreign institution because of the common illusion of the magical curative properties of the air and sunshine of some foreign health resort is deeply to be deplored. No patient who is suffering severely from the toxæmia of tuberculosis should be sent abroad. On the other hand, in the case of a wealthy patient whose acute systemic intoxication has subsided under treatment, but whose further progress has become unduly slow, a change of scene to Switzerland may be beneficial. There is no doubt that high mountain air has certain tonic and hæmopoietic properties, and the sunshine and novel surroundings often have a stimulating psychological effect. This may be more than counterbalanced, however, if the nursing in the foreign institution is inadequate, as it so often is. No patient should therefore be sent abroad who is not well enough to be out of bed for a part of the day and able to attend to some extent to his own requirements.

**Rest.**—In tuberculosis the traditional therapeutic triad—fresh air, good food and rest—has stood the test of time, but the greatest of these is rest. To give insufficient rest is the commonest error in treatment. A surgeon now appreciates the importance of rest in the cure of tuberculosis of the bones and joints more fully than the physician in the cure of the pulmonary variety of the disease. In this respect the surgeon is helped by anatomical features which may favour the easier acceptance by the patient of a long period of rest. Further, it is comparatively easy to immobilize a tuberculous knee joint in a plaster case, but it is impossible to immobilize a lung which expands and contracts in the process of breathing some 30,000 times a day. It is true that this immobilization can be accomplished to a great extent by collapse therapy (see p. 130). Rest in bed, however, is of primary importance in ensuring that the respiratory movements are sufficiently quiet and shallow to favour the formation of fibrous tissue.

The factors which contribute to the inadequate prescription of rest so common in the treatment of tuberculosis have been enumerated by Roche as follows :—

1. The doctor is often influenced by teaching which used to stress unduly the value of graduated labour and exercise of all kinds in the open air at an early stage in the disease. No doubt carefully graduated exercise and occupational therapy are most beneficial in the final stages of treatment, but they should not be started too soon.

2. The severe symptoms of tuberculous toxæmia often disappear under treatment long before the local lesion is sufficiently healed to make it permissible for exercise to be started. The patient therefore feels too well to



lie in bed, and the doctor too often yields to his importunities to be permitted more latitude. Patience on the part of both doctor and patient is perhaps the most important of all qualities in the treatment of tuberculosis. No intelligent person, however, can be expected to exercise this quality to the necessary extent unless the reasons for long-continued rest are carefully explained to him. The cultivation of a co-operative spirit between the doctor and the patient, and the psychological ascendancy of the former over the latter, are essentials of successful treatment.

3. Public or individual economic difficulties may militate against prolonged rest: an inadequate number of institutional beds may conduce towards hurried treatment, owing to the length of the waiting list; or private economic insecurity may unsettle a patient, so as to curtail the requisite period of treatment.

4. Perhaps the most important cause of insufficient rest in the treatment of tuberculosis lies in the inadequate appreciation of the criteria on which the control of rest is based. There is no single method which will give this information. The control of the case must be determined by weighing the evidence derived from a number of sources, the most important of which are: temperature, pulse-rate, weight, general symptoms, X-rays, blood sedimentation rate. The extent of the tuberculous lesion itself is no criterion of the amount of rest which should be prescribed. A patient with a small lesion may be seriously ill and in need of absolute rest, whereas extensive fibroid disease affecting both lungs may be no contraindication to a moderately active life.

*Temperature.*—A carefully kept record of the temperature taken night and morning is an essential in the treatment of all cases of active tuberculosis. Occasionally four-hourly recordings may be instructive. While the rectal temperature may be more accurate than the temperature taken in the mouth, its inconvenience makes the oral method preferable. Axillary skin temperatures are too inaccurate and should not be used. The thermometer should be kept in the closed mouth for at least three minutes, and no hot or cold foods or liquids should be taken immediately beforehand. It should be remembered that 98·4° is not a normal temperature for a patient who is confined to bed all day. In such cases the diurnal swing of the temperature should be below this level, and a chart which shows persistent readings along the so-called "normal" line indicates a mild degree of pyrexia.

A high swinging temperature is an indication for complete rest in bed. When the pyrexia is only moderate and there are no other contraindications the patient should be allowed up for toilet purposes, as this greatly conduces to his mental and physical comfort. Apart from this, however, rest in bed throughout the twenty-four hours should be the rule for a patient with exudative tuberculosis until the temperature has entirely settled. A few cases of chronic fibroid tuberculosis with cavitation invariably have an evening temperature of 99° or even 100°. A certain amount of latitude in the matter of exercise should be allowed such patients, whose management (see p. 127) is very different from that of the young adult with exudative tuberculosis. When the patient is allowed out of bed the temperature should be taken following exercise, and any instability of temperature at this time, especially a delay in returning to normal limits, will suggest caution.

While the temperature is a most valuable guide in determining how much rest or exercise should be prescribed, too much dependence should not be



placed on it alone. Some cases of progressive disease who are not fit to be out of bed may be practically apyrexial; on the other hand, an occasional small rise of temperature may be of little significance if other features are favourable.

*The Pulse-rate.*—As a general rule a resting pulse-rate of ninety per minute or over is an indication for the continuance of complete rest. A slow, steady pulse of good tension is a favourable sign. In most cases the temperature and pulse-rate rise and fall simultaneously, but in some the pulse remains elevated long after the temperature has become persistently normal or vice versa. In such cases the abnormal rather than the normal feature should be the controlling factor.

When exercise is started the pulse-test as used at Frimley is of value: the average resting pulse-rate is taken as being normal for the patient, who is then sent to take his prescribed amount of exercise; he lies down as soon as he returns and the pulse-rate is estimated immediately, and again in five minutes and half an hour. If a raised pulse-rate is due to mechanical cardiac embarrassment, such as may occur in pulmonary fibrosis or emphysema, the pulse-rate usually returns to normal in half an hour. If it is due to toxæmia, however, the tachycardia will be more persistent and will demand a reduction in the patient's activities.

Just as in the case of the temperature, the pulse-rate is simply a link, though a valuable one, in the chain of evidence which should govern the doctor's prescription of rest or exercise.

*Radiography.*—Good X-rays, supplemented by tomograph pictures when necessary, taken at regular intervals are more useful than the stethoscope in determining whether or not a patient is fit for exercise. The extension or limitation of the disease can be determined radiologically with considerable accuracy and furnish useful criteria for further rest or increased activity.

The X-ray appearances, however, must be interpreted in the light of the clinical picture. To make a prognosis from the X-ray picture alone is the worst possible practice. In this connection the use of X-rays is limited by the fact that it is not always possible to tell whether a shadow on the X-ray plate indicates active or healed disease. This is specially the case when many shadows are present. Further, foci of active disease may be concealed by the heart shadow, and the extent of their activity may not always be apparent even when lateral or oblique views are taken. Lastly, should a patient have a fibrous cavity in the lung, the radiological findings may not indicate whether or not he should be allowed to take exercise. This will depend on the presence and extent of toxæmic signs and symptoms.

*The Blood Sedimentation Rate* (for Technique see p. 850).—This test should never be omitted when any doubt exists as to whether a patient should be allowed out of bed or as to the amount of exercise he should be permitted to take. The test is so simple and easy to perform that there is no reason why it should not be widely used in general practice, where it will be found to have numerous applications.

Generally speaking, it may be said that patients with healed tuberculous lesions, and otherwise in good health, have a normal sedimentation rate (below 8 Westergren); in quiescent cases, and in fibroid tuberculosis without toxæmic symptoms, the sedimentation rate will be slightly accelerated (8 to 16); and in progressive cases—particularly where the disease is exudative in type—it may vary from 16 to 100, depending upon the severity of

the process. The test has thus the same significance in tuberculosis as fever, tachycardia and emaciation, but it may be a more sensitive expression of the activity of the disease than any of them. Thus an increased rate of sedimentation may be noted long after the temperature, pulse-rate and nutrition have returned to normal, and may sound a warning note against the premature prescription of exercise, just as it may do under similar circumstances in rheumatic fever. The sedimentation rate, however, is by no means infallible. We have occasionally seen patients suffering from active progressive disease with normal sedimentation rates.

Ideally, all patients with exudative disease who appear to have a reasonable hope of cure should be kept in bed till their blood sedimentation rate has fallen below 16, and preferably below 10. Thereafter, as long as the sedimentation rate, performed once a fortnight, keeps within normal limits, and provided the other prognostic data are satisfactory, the amount of exercise allowed can be steadily increased.

*Weight.*—The weekly weight of the patient is a useful guide to the progress of the disease, provided the various other factors enumerated above are taken into consideration. No patient should be allowed out of bed till the nutrition has become reasonably satisfactory, and a careful watch should be kept on the weight and on the muscular tone while exercise is being increased.

*Symptoms.*—The exacerbation of existing symptoms or the appearance of fresh ones such as dyspnoea, tiredness, increased cough or sputum, hæmoptysis, pleural pain or undue sweating requires an immediate re-assessment of the case and possibly a limitation of the patient's activities. The psychology of the patient must, however, be taken into account in assessing the significance of such symptoms.

In summary, then, a patient with exudative tuberculosis in whom there is a chance of obtaining arrest of the disease should be kept in bed till his temperature, pulse, nutrition, X-ray picture and blood sedimentation rate are satisfactory. Thereafter exercise should be very gradually increased in proportion as the prognostic criteria noted above continue to be favourable. It is far better to err by increasing exercise too slowly than too quickly. It is exceedingly disappointing to a patient who has reached a certain stage in treatment to have to curtail his activities or possibly to go back again to complete rest in bed. Finally, every effort should be made to induce the patient to cultivate some suitable hobby. There is nothing more conducive to morbid introspection than complete idleness.

*Fresh Air.*—Since the beginning of the century fresh air and tuberculosis have been spoken of in the same breath. In fact, they have been so linked together in people's minds that there has been a tendency to believe that open-air treatment is specifically beneficial for tuberculosis and for nothing else. This is entirely fallacious. There is nothing specific in the effect of open air on tuberculosis. The free exposure of a patient to fresh circulating air is of the greatest therapeutic value in raising his resistance towards any infection, particularly to respiratory infections. With a few exceptions all sick persons do better if they are nursed in the fresh air, provided conditions of heat and cold are not too rigorous, and provided shelter can be obtained against wind and rain. Old people, infants and patients suffering from a few diseases, such as acute nephritis, are exceptions to this rule. In many diseases, in which various forms of specific treatment

are employed, the use of fresh air as a therapeutic agent is often neglected. In tuberculosis, in which treatment largely consists in raising the resistance of the individual through natural means, the importance of fresh air has been well recognized.

Rest in the fresh air produces remarkable changes which have to be seen to be believed. Night sweating can almost be guaranteed to disappear in the first few days of open-air treatment. Sleep becomes sounder and more refreshing, provided the patient is not allowed to become chilled through insufficient bedclothes. The appetite, which is usually poor in untreated tuberculosis, is rapidly regained and may indeed become unusually keen. The temperature abates much more rapidly in the fresh air of a sanatorium than it does in the moderately fresh air of a ward in a general hospital. Cough and expectoration are diminished. Perhaps the most striking changes occur in the appearance of the patient, whose tissues regain tone and whose complexion improves. Shabby-looking people begin to bloom and even to become beautiful. As the patient experiences the tonic influences of fresh air and notices the disappearance of his symptoms, his mental state often improves as much as his physical condition. Hope returns and with it a determination to get well.

The benefits derived from fresh air are due to its cutaneous or physical properties rather than to its respiratory or chemical qualities; that is, the effects depend on the tonic influences of circulating air on the skin rather than on the chemical composition of the air breathed. A stuffy atmosphere is not usually detrimental to health because of its chemical constitution—such as an excess of  $\text{CO}_2$ —but because its air is stagnant and laden with moisture and possibly with pathogenic organisms. Thus the therapeutic effects of fresh air can often be obtained almost as well in a room as outside, provided the room can be thoroughly ventilated; and town air may be as beneficial as country air, provided it circulates freely and does not have to reach the patient in a small back court or down a shaft in the middle of a tenement.

To nurse a patient outside in a comfortable shelter or verandah ensures for him real open-air treatment. Such conditions are usually obtainable without inconvenience in a sanatorium or a country house. As we have seen, however, it is not essential to live outside in order to get fresh air, and many a patient in the town is put to great inconvenience by attempting to do so. He is much better in his own comfortable bedroom, provided it can be well ventilated, than in a shed in his back yard. His bedroom must have its window or windows open top and bottom, however, and the bed should be drawn across the window or otherwise arranged so that the patient obtains the maximum of fresh air. Curtains, hangings and furniture should be reduced to a minimum in his room. Many persons consider that sufficient fresh air is obtained by opening their bedroom window a few inches, and the doctor will have to make it quite clear that more than this is required. Further, he may find it difficult to get suitable conditions owing to the fear that the patient, or the members of the family who attend him, will catch colds or chills. He will have to explain that infections of this nature are never caught from fresh air. With perseverance the patient will soon constitute himself the doctor's best ally in this respect, as he will quickly become used to fresh air and finally intolerant of a stuffy atmosphere.

Cold air is no drawback to treatment. Young patients can habituate

themselves with benefit to most of the low temperatures encountered in this country, and can continue in open-air conditions throughout the winter. Indeed, after a little training they soon find the atmosphere of the ordinary household extremely oppressive. A fetish is, however, sometimes made of "hardening" patients. The writer has seen snow-drifts in the corners of sanatorium wards, and has encountered institutions where any form of heating in the wards, even a coal fire, was forbidden. Such rigours are quite unnecessary and only succeed in making patients unhappy; indeed, when applied to elderly or cachectic patients, they can do much harm.

Plenty of clothing is necessary for patients under a sanatorium regimen in cold weather, both for the person and for the bed. Such clothing should, however, be light rather than heavy. It is warmer and more beneficial to allow several light wraps rather than a single thick one. Shetland woollens are extremely suitable for this purpose, being warm and yet permitting the free circulation of air. In cold weather the hands of patients in bed should be protected by woollen gloves.

Heat, especially humid heat, should be avoided even more than cold. The bed, in hot weather, should be kept in the shade, and should be placed so as to get any breeze that may be present. Electric fans may be useful in such circumstances. The problem of excessive heat is not, however, a difficult one to cope with in this country.

While heliotherapy is undoubtedly of service in tuberculosis of the skin, glands, bones and joints, it has probably no value in pulmonary tuberculosis. Any benefit claimed from exposing the chests of patients with chronic pulmonary tuberculosis to sunshine is most likely due to the stimulus of fresh air on the skin or to psychological causes. In active exudative cases heliotherapy is definitely contraindicated and may have detrimental effects, comparable to an excessive dose of tuberculin. Such patients should therefore be guarded against direct exposure to strong sunshine in the summer time.

Patients frequently inquire whether smoking will interfere with the benefits of open-air treatment. Since fresh air, as we have seen, produces its effects through its action on the skin rather than through the lungs, it is improbable that smoking will be harmful from this point of view. It is our custom to allow patients with pulmonary tuberculosis to smoke in moderation, provided laryngitis or bronchitis is not a feature of the case and provided the cough is not obviously aggravated by smoking, as is occasionally the case.

**Diet.**—A large number of dietetic systems have been recommended from time to time as specifics in the treatment of tuberculosis. These range from the excessive or even forcible feeding of consumptives which was in vogue about the turn of the century to the Gerson-Sauerbruch diet introduced during recent years. Fishberg has said with truth that a good cook is more useful in the management of a tuberculous case than a detailed diet sheet. It is, indeed, unwise to lay down strict dietetic rules applicable to all cases of tuberculosis, since the individual's economic position, his likes and dislikes as regards food and the state of his digestion should all be taken into consideration in arranging his diet. None the less it may be helpful to consider certain broad general principles as regards dietetics in tuberculosis, though it is well to remember that in tuberculosis no dish is definitely contraindicated provided the digestion is good.

Since tuberculosis is a wasting disease, and many of the patients who suffer from it are in addition poor and undernourished, it is plain that on the whole more food should be given to tuberculous than to ordinary people. On the other hand, the grossly excessive feeding which used to be so popular only succeeds in causing dyspepsia, and the patient should never be forced to take more food than he wishes. Three good meals a day are sufficient. In addition there is no objection to a small tea, and a glass of milk may be taken before going to sleep at night. Otherwise small feeds in between the principal meals should be discouraged as being detrimental to appetite and likely to cause dyspeptic symptoms.

As wasting of muscle is a common feature of active tuberculous disease, it is important to see that the diet contains an adequate amount of animal protein in the day; otherwise a negative nitrogen balance is apt to occur. There is no need, however, to stuff the patient with huge quantities of expensive protein food. The administration of 1.5 gm. of protein per kilogram of body-weight is sufficient to prevent a negative nitrogen balance in all cases of tuberculosis. This protein intake will be ensured provided the patient takes a good helping of meat and fish, an egg and a pint of milk in the course of the day.

Tuberculous patients should have plenty of milk. At least 1 pint and preferably 2 pints should be taken daily. Many patients protest that they cannot take milk. This is in the great majority of cases a fad with no foundation, but, unfortunately, occasional cases of true milk intolerance do occur. In such patients the drinking of milk is invariably followed by abdominal discomfort, flatulence and sometimes diarrhoea.

Protein will not fatten a patient, and a diet containing plenty of fat has been recommended from the earliest times in the treatment of tuberculosis and is probably beneficial. It must be remembered, however, that many patients are intolerant of large amounts of fat, which may produce nausea and gastro-intestinal disturbances. It is useless to attempt to give fat in large amounts to such patients. Butter is probably the most easily assimilated form of fat and can usually be taken freely. Fat fish such as herring, salmon, fish roe, mackerel and sardines are also useful sources of fat which are generally well borne. Those who can tolerate fat easily can take in addition cream, fat bacon, ham and other fat meats. For generations cod-liver oil has been looked upon as a sheet-anchor in the treatment of tuberculosis. It is a rich source of fats and of vitamins A and D. Fat can, however, be given in much more palatable forms, and provided a good mixed diet is being taken there is no reason to believe that tuberculous people are peculiarly liable to vitamin A and D deficiency. The old theory that demineralization occurs in tuberculosis has never been proved, and there is no trustworthy evidence to show that the calcification of tuberculous lesions is accelerated by the administration of cod-liver oil. Cod-liver oil should be prescribed, especially in winter, to those indigent people who can tolerate it and whose diet may not be adequate in fats or vitamins. The pure oil should be taken in amounts varying from  $\frac{1}{2}$  to  $1\frac{1}{2}$  oz. a day. If patients dislike the pure oil, concentrates of vitamin A and D can be used (see p. 407).

The diet should contain plenty of fruit and green vegetables. All patients who suffer from chronic fevers require more vitamin C than healthy persons, and patients who have a tuberculous pyrexia are no exception to this rule.

In such cases the diet should be supplemented by 150 mg. of ascorbic acid a day. This is particularly necessary at present when the diet may lack an adequate quantity of vitamin C. Even this dose may be insufficient for patients suffering from a long-continued hectic temperature, whose vitamin C requirements may be as high as 300 mg., or, in extreme cases, 500 mg. a day.

An excess of starchy carbohydrates should not be taken. If large quantities of white bread, cereals, pastries and sweets are eaten the patient may not have any appetite left for the more protective foodstuffs. Further, there is some evidence to suggest that an excess of carbohydrate food may accelerate the spread of the exudative process in the lung.

On the other hand, it has been suggested that patients who fail to gain weight may be assisted by the injection of soluble insulin followed by large doses of glucose. Doses of 10 units of soluble insulin twice a day are usually ineffective, but a considerable gain in weight is often achieved by keeping the patient in an almost continuous state of mild hypoglycæmia, by three or four injections a day of from 12 to 16 units. Each injection is followed by the administration of glucose, and frequent meals with a high carbohydrate content are given. The pathological state of hunger produced by the insulin makes the patient very ready for meals. This treatment is extremely unpleasant on account of the numerous injections involved and the continued sensations of hypoglycæmia produced. Further, the weight gained is seldom maintained once the treatment is discontinued, and it is doubtful whether any permanent benefit accrues.

Extra nourishment can be obtained for necessitous cases by application to the local tuberculosis authorities. At present patients suffering from active tuberculosis of all types are allowed two pints of milk a day by the Ministry of Food.

**After-care.**—When a patient's disease has become quiescent, or when he has become sufficiently well to be discharged from a sanatorium, he should none the less continue under medical supervision. The family doctor, in conjunction, perhaps, with the local tuberculosis authorities, should keep a close watch upon him. To begin with, he should report for clinical examination at least once a month. Ideally, a blood sedimentation test should be performed at the time of the examination, and a radiological examination should be made every three or four months during the first year of convalescence. It will depend on the patient's temperament as to whether he should be asked to keep a chart of his temperature during this time. Such a record is useful in diagnosing at an early stage a possible recrudescence of the disease. On the other hand, the continual taking of the temperature may be a factor in inducing a hypochondriacal state in the patient. For the unduly optimistic type of patient continual warnings may be necessary. The well-known *spes phthisica*, however, is by no means universal, and many patients are morbidly introspective and anxious about themselves. These latter require much encouragement and reassurance from their doctor, who should make every effort to stop them from brooding on their disease. It is usually unwise to ask such patients to keep a temperature chart.

Provided a patient has been fit for a full amount of exercise for some time, and provided the various prognostic criteria enumerated above continue to be satisfactory, a return to work should not be unduly delayed. A

patient kept idle for too long is apt to become introspective and neurotic or lazy and unemployable.

On first returning to work, the patient should be warned that he should spend the time in resting which others spend in recreation. Thus the ordinary division of the twenty-four hours into eight hours' work, eight hours' play and eight hours' rest should for him be divided, as far as possible, into eight hours' work and sixteen hours' rest. It may occasionally be wise to advise him to stay in bed entirely on Sunday.

Further, the patient must be warned against reverting to bad habits as regards inadequate fresh air. He should avoid as much as possible stuffy, crowded atmospheres, such as are often found in cinemas and theatres, and should take every precaution against contracting upper respiratory tract infections (see p. 722). A cold in the head should be treated seriously by him and he should go to bed till the worst of the infection is over.

Finally, every effort should be made to see that meals are ample and well cooked. The hurried consumption of small starchy meals at snack counters should be avoided.

**Employment.**—The question will at once arise as to what sort of work he should undertake; if at all possible he should return to his original employment. There are, of course, certain forms of employment involving great physical exertion, or work in dusty atmospheres and in extremes of heat and cold, which are manifestly unsuitable for people who have suffered from tuberculosis. Likewise, when a woman's employment brings her into close contact with young children, as, for instance, in the case of a teacher in an infant school, or when the work involves contact with food, as in the case of a dairymaid, new employment will have to be sought.

Apart, however, from these obviously unsuitable vocations the patient should attempt to return to his or her original employment. Even when this is not entirely suitable from a tuberculosis point of view, it is much less strain for the patient to do the work to which he is accustomed than to attempt an entirely new occupation in strange surroundings for which he may be totally unsuited.

It should be remembered that it is more important for a tuberculous individual to obtain sedentary work rather than work in the open air, though light work in fresh air is the ideal. Too often a bank clerk is advised to become a chicken farmer, an occupation which may involve much physical exertion and for which he may have no aptitude.

**Marriage.**—The practitioner will sometimes be asked as to the advisability of one of his tuberculous patients marrying. Provided the healthy partner understands thoroughly the implications of marrying a person who has, or has had, tuberculosis, marriage may be beneficial in some respects to the patient. Thus a man may have a more restful and comfortable home with better-cooked meals than he had when a bachelor; and a tuberculous woman, who has had to earn her own living previously, may obtain protection, security and possibly an easier life through matrimony than she had when single. On the other hand, matrimony may increase a man's responsibilities necessitating harder work for him, and it may well be the beginning of an anxious and strenuous life for a woman. It all depends on the circumstances of the case, and on the position and mentality of the persons concerned. These matters will have to be taken into consideration by the practitioner in coming to a difficult decision.



In any case, no tuberculous person should marry unless the healthy partner is fully conversant with the tuberculous history. The risks of a possible breakdown in health and of the patient's physical capabilities should be explained fully to the fiancé, with whom the family doctor should have a private interview. No woman with tubercle bacilli in the sputum should have a baby. Pregnancy may be borne reasonably well owing to the fact that in the later months the uterus progressively pushes up the diaphragm and an effect is produced similar to a phrenicectomy. Active disease, however, tends to progress disastrously during the puerperium when the diaphragm descends and moves freely again. Further, the risks which an infant runs under such circumstances of fatal infection from its mother are very great. So great, indeed, are the dangers of pregnancy to a woman with active exudative pulmonary tuberculosis that therapeutic abortion may be considered if the pregnancy has not progressed beyond the third month, and if the disease cannot be satisfactorily controlled by an effective pneumothorax. It is probably inadvisable for a woman to start a family for at least two years after her sputum has become free of tubercle bacilli, her symptoms in abeyance and the various prognostic tests satisfactory. Naturally these implications will have to be carefully explained to the woman's fiancé. There is no reason why two tuberculous people should not marry provided their circumstances are such as to make it possible for them to live an easier life married than single.

**Chronic Fibroid Pulmonary Tuberculosis.**—The management of a case of chronic fibroid tuberculosis provides a very different problem from that presented by a patient suffering from exudative disease. When the chronic disease is unilateral, the patient may often be saved from permanent invalidism by one or other of the methods of collapse therapy—particularly thoracoplasty (see p. 138). The feasibility of inducing collapse must, therefore, be seriously considered in all unilateral cases. Collapse therapy is, however, often impracticable in advanced chronic disease affecting both lungs. In such cases all that can be done is to regulate the life of the patient so as to keep his activities as far as possible well within the bounds imposed by his limited capacity, to treat symptoms as they arise (see p. 139), and to attempt to prevent him from infecting other people by giving him advice as to personal hygiene and by keeping him from close contact with children (see p. 112).

In some cases a considerable degree of systemic intoxication may be present owing to the retention of secretions in fibroid cavities and in collapsed portions of lung. Where toxæmia is marked, the patient must be kept in bed, and the general measures adopted must approximate to those already mentioned. It is usually unnecessary and unwise to send such patients away from home to an institution. Far too many beds in sanatoriums are occupied by elderly patients suffering from chronic, fibroid phthisis, sometimes to the exclusion of early and curable cases. Where, however, the home conditions are obviously unsuitable for proper nursing, or where young children are present in the house, it may be necessary to segregate the patient in a hospital for advanced cases. The principles as regards rest in bed, which have been recommended for curable cases, need not be applied so rigidly to patients with advanced chronic disease. They are often happier, and indeed better, if they are allowed to be up for a short time each day, usually in the morning when their temperature may be



normal and when they feel at their best. Much can be done to make them more comfortable by careful treatment of their symptoms. Such treatment is described later (see p. 139).

When a patient first develops pulmonary tuberculosis, the chances of his dying within five years are considerable. If he lives for five years, however, his chances of survival for a further period are proportionately greater. He has proved himself resistant to the disease, and even though it persists it usually becomes progressively less virulent and less toxic, though at any time it may extend within the lungs or elsewhere in the body. Thus, the longer a patient survives, the less he tends to suffer from the systemic effects of tuberculous toxæmia, and the more from the effects of pulmonary fibrosis, complemental emphysema and right-sided cardiac embarrassment. Thus extensive fibroid disease, even when associated with gross cavitation, is not necessarily inconsistent with many years of useful and moderately active life. Systemic intoxication is minimal and the patient frequently lives almost in symbiosis with his tubercle bacilli, suffering to a greater or less degree from cough and dyspnoea on exertion, but otherwise feeling comparatively well. Many of them are able to attend to their work and businesses, and should not be prevented from doing so. Their treatment should be very similar to that suggested for patients suffering from chronic bronchitis and emphysema (see p. 736).

### TUBERCULIN TREATMENT

Under the influence of rest, fresh air and good food the majority of patients suffering from pulmonary tuberculosis show some improvement; whereas, if they do not receive these benefits the majority get worse. We *know*, therefore, that these are useful methods of treatment in tuberculosis. The same cannot be said for other forms of treatment, for, with the exception of collapse therapy, which is simply an extension of the principle of rest, none of them gives good results with any constancy. It is, indeed, exceedingly difficult to gauge the effect of any remedy in a disease which may last a lifetime, which is subject to natural fluctuations in severity and to the strongest tendency to spontaneous healing under an ordinary physiological regimen. Further, many patients suffering from tuberculosis are highly suggestible and will react favourably to any harmless drug, or even to distilled water if it is administered with impressive gravity, especially by the hypodermic route. This favourable reaction will be magnified if the administrator himself believes firmly in the efficacy of the nostrum and is able to impart his faith in it to the patient. Hence, tuberculosis, like disseminated sclerosis, is a happy hunting-ground for the uncritical therapeutic enthusiast and for the "quack."

Among serious workers opinion is unanimous that there is as yet no specific remedy for tuberculosis comparable to quinine in malaria, sulphonamides in pneumonia or antitoxic serum in diphtheria. Here, however, unanimity ends, and controversy is particularly acute in regard to the efficacy of tuberculin treatment. More than sixty years after its introduction by Koch as a remedy for tuberculosis, a small and diminishing band of workers remain fanatical exponents of its excellence, while another, and much larger group, as hotly proclaim its therapeutic worthlessness.

Until about fifteen years ago there were many forms of tuberculin on

the market, but waning belief in its value as a therapeutic agent has led to their gradual disappearance, and to-day Koch's original Old Tuberculin is practically the only form used. The newer purified protein derivative (P.P.D.) is used only in diagnosis. In all tuberculins the essential constituent is a protein derived from the growth of tubercle bacilli in liquid culture media, and it is that protein which elicits in those who have been infected with tuberculosis the reactions which are characteristic of the allergy of the disease. In moderate doses tuberculin is without effect on non-infected persons. In those who have been infected it causes reactions of three types: the local, which is the basis of the tuberculin test; the general, which is characterized by fever and malaise and is due to the absorption of tuberculin into the blood stream; and the focal, which is represented by hyperæmia and inflammatory changes around existing foci of tuberculosis in the body. If the dose of tuberculin is sufficiently large these latter reactions may be intense and may lead to extensive breakdown and spread of the tuberculous lesion. Focal reactions are easily observed in tuberculosis of the skin and eye, and the value of tuberculin in treatment was thought to depend upon these reactions. The theory that mild controlled reactions of this nature lead to healing of the lesions is probably erroneous, but where the lesions are under direct observation the dosage is under some measure of control. In pulmonary tuberculosis there is no such direct observational control, and the danger of causing uncontrollable reactions is so great that tuberculin has been practically abandoned in the treatment of this condition.

Relative immunity to tuberculosis can be produced (see B.C.G., p. 113), but only by the injection of the whole tubercle bacillus. None of its hitherto isolated fractions, of which the tuberculo-protein is one, has any immunizing effect and the employment of tuberculin for that purpose is useless. It is now accepted that the allergy of tuberculosis is distinct from immunity and is responsible for the caseation and many of the complications and symptoms of the disease. As such it is an undesirable phenomenon. The specificity of tuberculin in eliciting the allergic response suggests its use as a desensitizing agent, and there is no doubt that skin sensitivity can be greatly reduced, and even abolished, by a prolonged course of tuberculin injections. That is the probable mode of action of tuberculin, and theoretically it should be of value in all forms of chronic tuberculosis. The criteria of control are, however, clinical, and to that extent varying and inexact, and it is unwise to employ tuberculin in deep-seated and hidden forms of the disease where the slight reactions on which dosage depends are determined with difficulty or not at all. It is accordingly better to confine its use to glandular tuberculosis, to lupus and to the genital forms of the disease in the male. Its use in renal tuberculosis and tuberculosis of the eye should be left to specialists in these branches of medicine. (For Technique see p. 152.)

### DRUG TREATMENT

**Gold.**—Many of the remarks which have been made about the efficacy of tuberculin apply equally to gold in the treatment of tuberculosis. There can be no doubt as to its dangers but there is great dubiety as to its efficacy. It is generally agreed that gold is of no service in chronic fibroid cases and that it is contraindicated in cases of acute exudative disease with severe toxæmic symptoms. It is advocated in exudative or fibro-caseous

cases when toxæmia is mild, or absent, and when the disease is slowly progressing. In some cases it certainly appears to cause the disappearance of tubercle bacilli from the sputum and to reduce its quantity, but on the whole gold is used much less now than was the case fifteen or twenty years ago in the treatment of tuberculosis.

If gold has a beneficial effect, its mode of action is not clear. Almost certainly it has no bactericidal effect on tubercle bacilli within the body, though very weak solutions of gold salts will inhibit their growth in culture. It is supposed to stimulate the defensive forces of the patient and to increase the tendency to fibrosis in tuberculous lesions.

The method of giving gold in tuberculosis does not differ from that employed in rheumatoid arthritis. The preparations used, their dosage, the technique of their administration and their toxic effects are fully described on p. 811, to which the reader is referred.

**Other Drugs.**—Neither the sulphonamides nor penicillin have a specific effect in tuberculosis.

Within recent years a phenyl sulphone named promin in America and promanide in this country was found to exert a bacteriostatic effect on tubercle bacilli in vitro and a retarding effect on experimentally produced tuberculosis in guinea-pigs. Promin is too toxic for prolonged use in human beings and two other members of the group, promizole and diasone, were tried. Both have the same effect on experimental disease as promin, but both are less toxic and diasone, the least toxic of the three, has been tried on small groups of patients suffering from pulmonary tuberculosis. Even with its toxic effects were troublesome and the published results of the trials are unconvincing.

Streptomycin, an antibiotic prepared in 1943 from *actinomyces griseus*, has given striking results in experimental tuberculosis. It is difficult and costly to produce in a pure state, but it is much less toxic than the sulphone drugs and experimental results have suggested that it might be of value in certain types of human tuberculosis. It is undergoing official trials in this country and results must be awaited. The results of a comparatively small series of patients treated in America have shown that the drug has an effect in controlling certain acute forms of tuberculosis and that it can modify the course of chronic pulmonary tuberculosis. It is given by injection at four to six hourly intervals over periods of several months, but even in patients who benefit from it improvement is slow and its sphere of usefulness is likely to be that of a supplement to existing approved methods of treatment. It is not at the time of writing available for private use.

Numerous other drugs have been advocated from time to time in tuberculosis: creosote, arsenic, iodine, sodium morrhuate, calcium and parathyroid extract. They have all had their day and have been found wanting. Apart from preventive measures, the only great advance so far made in the treatment of tuberculosis since the introduction of rest and the sanatorium régime has been collapse therapy, though specific chemotherapy seems almost within sight.

D. M. DUNLOP.

### COLLAPSE THERAPY

Many cases of pulmonary tuberculosis remain active or tend to progress in spite of strict sanatorium treatment. Failure to heal may be due, *inter alia*, to poor resistance, to the type of the disease, or to secondary mechanical

factors, and each requires careful individual assessment. In the lungs, as in other structures, healing is favoured if sustained physiological rest can be secured, and for that purpose there are now available for selected subjects a choice of several measures known collectively as *collapse therapy*. The value of collapse therapy is definitely established, and its use should not be withheld if the proper criteria for its application are present.

The specific effect of all forms of collapse therapy is the reduction of lung volume regionally or generally, with resulting diminution of tension (atmospheric and mechanical), so that reparative processes may not be inhibited or, if already present, can proceed unhampered. The methods used are:—

1. Artificial pneumothorax.
2. Intrapleural (cautery) division of adhesions.
3. Phrenicectomy (crushing or evulsion of the phrenic nerve).
4. Pneumoperitoneum.
5. Extrapleural pneumothorax.
6. Thoracoplasty (local or extensive resection of the ribs).
7. Resection of a diseased lobe or lung.
8. Drainage of cavities (Monaldi).

Omitted from this list are certain other operations such as oleothorax, scalenectomy and apicolysis with paraffin plombage, which at one time enjoyed an ephemeral popularity.

**General Indications and Choice of Method.**—The appropriate method of collapse and the time for its adoption depend on the special pathological conditions within the lung and pleura; each case must be decided on its individual features. Haphazard interventions will be avoided if the operator has ascertained the full history of the case—clinical and radiographic. The simpler methods, such as artificial pneumothorax, are employed in early and progressive cases in which the lesion will be of the exudative or caseous type. The more drastic measures which involve rib resection are reserved for established fibrotic disease, especially when cavity formation predominates. Sometimes the methods are employed in combination, *e.g.*, artificial pneumothorax and phrenicectomy with pneumoperitoneum may be combined advantageously in certain circumstances.

Troublesome symptoms, such as persisting irritating cough and recurring hæmoptysis, irrespective of the type of disease, may be controlled by artificial pneumothorax or phrenicectomy, even though the prospect of cure of the underlying disease is unlikely.

In the selection of cases there are certain rules and limitations which apply broadly to all methods of collapse therapy. Early and exudative cases present an urgent problem in treatment, whereas the patient with chronic fibroid disease does not suffer by reasonable delay. The prospects of success are greatest when the disease is unilateral, although in special circumstances, to be defined later, limited retrogressive disease in the healthier lung need not contraindicate such treatment. Active and extensive bilateral disease is an obvious barrier to treatment, though the introduction of bilateral collapse has greatly widened the scope of therapy even in such cases. The patient's age must be taken into consideration: the simpler methods may give very gratifying results in young subjects, even children, but thoracoplasty should be avoided before the age of seventeen years as scoliosis is apt

to follow. When there is myocardial weakness, emphysema and bronchitis, collapse therapy aggravates dyspnoea and should not be attempted. In consequence, these methods have a rather more limited scope in subjects over the age of forty-five.

Intercurrent disease does not necessarily preclude treatment. For example, many patients who suffer from diabetes as well as tuberculosis derive benefit from collapse, and their insulin requirements may be notably reduced. Complications, however, such as tuberculous enteritis or tuberculosis of the kidney or of the bones and joints are, with few exceptions, a contraindication to this mode of treatment. Ulceration of the larynx is an indication rather than a contraindication.

As there is still a significant mortality from all types of thoracoplasty, this major procedure must not be undertaken unless the patient's condition fully warrants its performance.

**Artificial pneumothorax** is the simplest means of producing lung collapse, and more complete collapse is attained by this than by any other method, provided adhesions between the visceral and parietal pleura are not present. In many cases it is only by trial that the efficacy of the method can be tested.

Artificial pneumothorax should be carried out in all but the very earliest cases of acute or subacute exudative tuberculosis of a unilateral nature, irrespective of whether there are gross physical signs or tubercle bacilli in the sputum. It should be used, too, in less acute cases in which activity persists in spite of rest in bed, or when the disease in the lung remains stationary, and especially if constitutional improvement is not satisfactory. Cavity formation is a common sequel of caseation and should be regarded as an indication for timely control by pneumothorax. There is less urgency in the more chronic and usually fibroid type of case, yet chronic invalidism need not be accepted as the inevitable culmination of the disease; an attempt should be made to induce pneumothorax, though it may not always be possible nor completely effective; not infrequently, if it is supplemented by other measures, such as division of adhesions or phrenicectomy, a successful issue may be attainable. With an effective pneumothorax the recovery of the patient may be accelerated and the risk of subsequent relapse diminished.

Enthusiasm for such treatment must be tempered with discretion because, on the one hand, there are certain early cases which may respond favourably to routine treatment and, on the other, fulminating types which are doomed from the outset. An experienced clinician will usually be able to anticipate the behaviour of any particular type of disease. A difficult problem arises when there is widespread acute disease in one lung and similar though less extensive disease in the other. The decision to induce pneumothorax on the worse side is based on the hope that reduction of toxæmia may bring about such improvement in the patient's general condition that the disease in the contralateral lung may improve. It is a reasonable gamble, but unfortunately the disease, especially if of the acute type, is sometimes aggravated.

Experience has now shown that an ineffective pneumothorax constitutes a real menace to the patient, and that if it cannot be made effective by the division of adhesions or by phrenicectomy it should be abandoned and an alternative method of treatment adopted. This is especially true when a

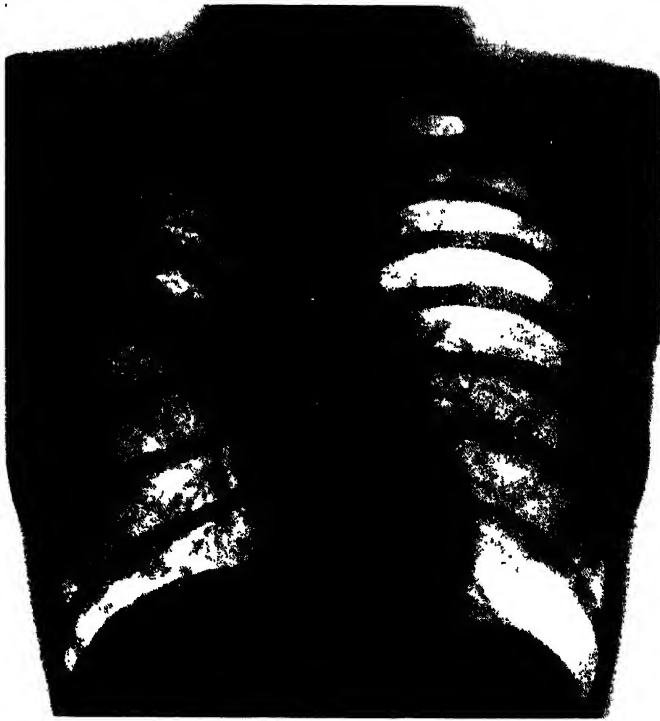


PLATE 1 Unilateral exudative pulmonary tuberculosis affecting right upper lobe. There is a small sub-axillary cavity, and a larger one opposite the root of the lung.

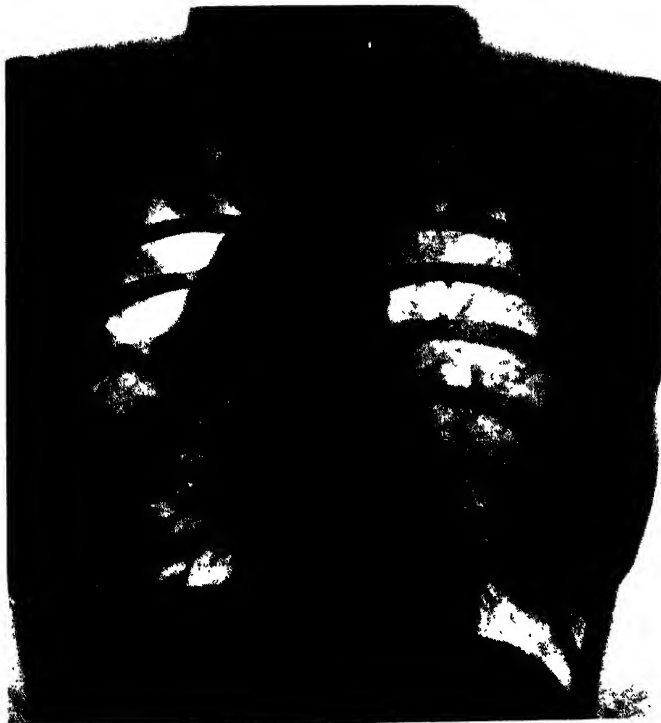


PLATE 2—Same case four months after the induction of artificial pneumothorax. A good selective collapse has been secured. There is a small pleural effusion.

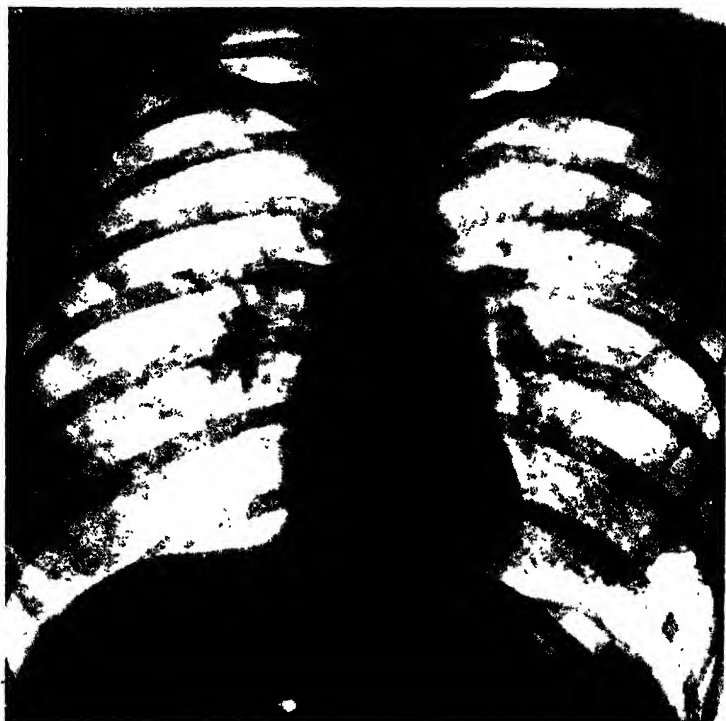


PLATE 3—Moderately active bilateral pulmonary tuberculosis.



PLATE 4—Same case two years later. Bilateral pneumothorax has been established, both lungs being concentrically collapsed.

large cavity remains inflated or increases in size in spite of an adequate pneumothorax.

*Bilateral Artificial Pneumothorax.*—There are many instances in which it is necessary to employ pneumothorax collapse in both lungs concurrently, and bilateral pneumothorax is often the only means of successful control of the disease. The following are the types of case in which it should be considered : (1) those in which there is already good pneumothorax control in one lung but slight or moderate disease has persisted (or has appeared) in the opposite side; (2) those in which at the outset moderately extensive disease of about equal extent is found in each lung.

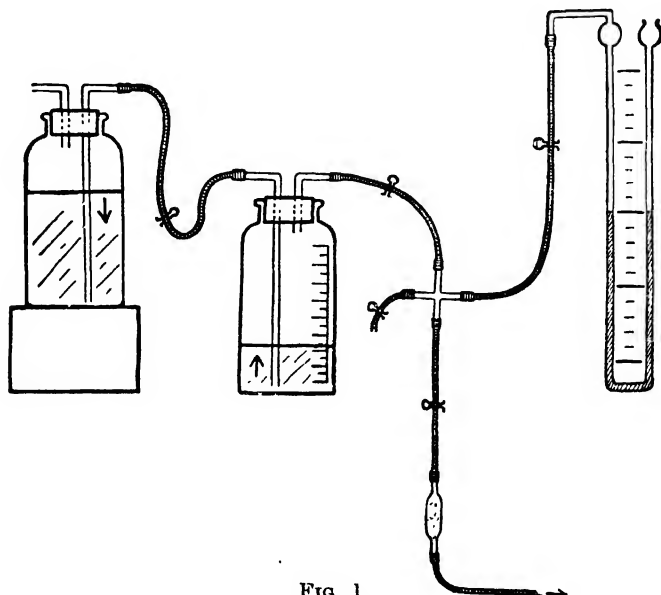


FIG. 1

Diagram to illustrate the principles of the Lillingston and Pearson artificial pneumothorax apparatus. Water, flowing from the left-hand (upper) bottle to that on the right, displaces air which is driven via hollow tubing and a cotton-wool filter to the needle in the patient's chest. A side tube leads to a water-manometer. Reversal of the bottles enables air to be withdrawn from the chest.

In the management of bilateral artificial pneumothorax it is usual to secure as perfect a collapse as possible on the one side before intervention on the other. The refills are given at such intervals as are found from screen examination to hold the optimum collapse without dyspnoea.

In a few cases artificial pneumothorax may be combined with a circumscribed thoracoplasty done for a persisting upper lobe cavity in the opposite lung.

*The Induction and Management of Artificial Pneumothorax.*—The simplest type of apparatus consists of two bottles, the one syphoning fluid into the other. Air is thereby displaced from the second bottle through a rubber tube and needle into the pleural cavity. The second bottle is graduated in hundreds of cubic centimetres, and the amount of air displaced can, therefore, be read off by the rise of the fluid level in the bottle. A water-manometer is always in connection with the apparatus, so that the intrapleural pressure can be ascertained at any moment.



The technique of induction follows the lines of paracentesis in general and is carried out under local anæsthesia (2 per cent. procaine), particular care being taken to infiltrate the sensitive pleura. The point of initial puncture is decided by the distribution of the disease as portrayed in the X-ray film. The fourth intercostal space in the mid-axillary line, or the sixth or seventh space in the scapular line, are favourite sites. A special pattern of induction needle is employed.

A successful entry into the pleural space is registered by the respiratory oscillations in the manometer, and in no circumstances should air be allowed to enter until an unequivocal oscillation is obtained. Continued failure to procure such oscillations is an indication to try elsewhere. When, from the manometer readings, it is certain that the needle is between the pleural layers, 50 to 100 c.c. of air are allowed to enter by aspiration; confirmatory pressure readings are taken before a total of 300 c.c. are admitted. The intrapleural pressure should remain negative. A positive reading suggests adhesion of the lung and should be a signal for caution or for abandoning further attempts.

If induction has been successful and the X-ray appearances and pressure readings are satisfactory, a refill may be given the following day. Thereafter, refills are continued at short but gradually lengthening intervals. It is usually about a month before the optimum collapse is established. Then the interval between refillings varies with each patient according to the rate at which the air is absorbed. The X-ray appearances are the most reliable guide in arriving at a decision. In an average case refilling at ten or fourteen day intervals is necessary at first, but as the rate of absorption decreases the interval can often be extended to three weeks or a month.

It is most desirable that the early stages of pneumothorax treatment should be undertaken in a sanatorium where the patient may be observed carefully from day to day. The refilling of a well-established pneumothorax is, however, a simple out-patient procedure to which the patient soon becomes habituated, regarding it no more seriously than he would an intramuscular injection. Provided a fine needle is used with dexterity, local anæsthesia is superfluous.

Treatment should be continued, even in the most favourable cases, for at least two years, and for three or more when the disease has been extensive or cavities present. The patient should be warned of this before starting treatment. Sometimes termination of treatment is decided by the behaviour of the pneumothorax itself—either by its progressive shrinkage or its obliteration by adhesions.

When the lung is allowed to re-expand it is safer to let it be gradual by spacing the refills at longer intervals and by reducing the amount of air given. Six to twelve months are usually necessary to achieve full re-expansion, and the patient should be kept under careful clinical and radiological observation throughout.

*Incidents during Treatment.*—Pleural shock is a very rare but disturbing effect of puncture of the parietal pleura. The symptoms vary from faintness and pallor to profound collapse, with, in exceptional cases, sudden death. Its occurrence has been attributed to incomplete anæsthesia of the pleura, but proof of this is lacking. The phenomenon is seldom witnessed after the initial puncture of the pleura. Treatment is on the same lines as for shock.

Air (gas) embolism resembles pleural shock in its manifestations, but is quite different in origin. It results from the entry of air into the pulmonary veins and its passage as emboli to the coronary or the cerebral arteries. Death may be immediate, or there may be epileptiform fits, hemiplegia or profound unconsciousness. In rare cases it may be survived. Air embolism should be extremely exceptional if it is always ascertained that the pneumothorax needle is within the pleural cavity by the characteristic oscillations in the manometer.

Subcutaneous emphysema is due to escape of air into the subcutaneous tissues via the puncture in the pleura. It produces a characteristic "crackling" sensation to the examining hand; but apart from the mild discomfort and annoyance it occasions, it calls for no concern. It is prevented if the induction of a positive pressure within the pleura is avoided, following upon a refill, and coughing discouraged.

Displacement of the mediastinum may occur when the mediastinal septum is more yielding than is usually the case in chronic inflammatory diseases of the chest. It may develop even when a negative pressure is present in the pleural cavity. The common effects are dyspnoea, tachycardia and loss of weight. The condition seldom calls for interruption of treatment. It can usually be corrected by reducing the volume of air given and shortening the interval between each refill.

Pleural effusion is a very frequent complication of artificial pneumothorax. It is the expression of a tuberculous pleurisy. It is more common in acute disease when adhesions are present, and though it may appear at any stage of treatment it generally occurs in the early months. The onset of an effusion is indicated by malaise, pain and a sharp rise of temperature which may last for a few days or sometimes weeks. If the effusion is copious there may be dyspnoea. A pleural effusion is not necessarily an untoward occurrence, and in the majority of cases it disappears spontaneously. In consequence, expectant treatment is usually indicated. Aspiration of a pleural effusion is required in the following circumstances:—

1. When there is long-continued pyrexia.
2. When it is of such bulk that it produces pressure symptoms.
3. When its long delayed absorption is likely to cause gross pleural thickening or obliteration of the pneumothorax.

Following aspiration of a large pleural effusion, re-expansion of the lung should be prevented by replacing the fluid with air (see p. 145).

In a small proportion of cases an effusion becomes purulent—pyopneumothorax. This is a serious occurrence and is usually an indication to abandon the pneumothorax. Periodic aspiration of the fluid should be carried out and re-expansion of the lung encouraged. Expansion of the lung may be long delayed and may sometimes be hastened by paralysing the diaphragm. It may be necessary finally to obliterate the persisting cavity, and to control underlying disease, by thoracoplasty.

A graver situation arises when there is a superadded pyogenic infection of the pleura (infected pyopneumothorax). Toxæmia is severe and persistent and cannot be checked by repeated aspiration. It is necessary to carry out an air-tight drainage of the pleural cavity and to attempt its disinfection by irrigation. The outlook is often (though by no means always) unfavourable. The use of penicillin intrapleurally (see p. 92) may bring about remarkable

improvement in the patient's general condition and eliminate the need for drainage. Thoracoplasty may be required subsequently.

Careful adherence to the following principles would do much to reduce the incidence of massive effusions and empyema in the course of pneumothorax treatment. Prompt termination of ineffective pneumothoraces; early division of adhesions in suitable cases; the recognition of the fact that in certain cases which require collapse pneumothorax is not necessarily the initial method to be used as a routine measure prior to thoracoplasty. Sometimes pneumoperitoneum is a more suitable preliminary treatment, especially in very acute active disease. Occasionally thoracoplasty is the method of choice at the outset, especially if the lung is the seat of a "giant" cavity.

**Intrapleural Division of Adhesions (Internal Pneumolysis).**—Adhesions may be unimportant, but often they prevent relaxation of the diseased parts of the lung or closure of cavities. As adhesion formation is a sequel to an inflammatory process in the pleura, it follows that it will be found most usually over the site of the pulmonary lesion and will therefore exert its influence where it is least desired. In such cases artificial pneumothorax may have had promising effects in the early stages of treatment, but disappointment follows because continued activity of the disease is suggested by such symptoms as cough, expectoration, hæmoptysis or by persisting systemic disturbance.

If, after a reasonable time (say two to four months), it can be demonstrated that adhesions interfere with an otherwise satisfactory collapse, and especially if cavities persist or increase in size, the division of the adhesions should be considered. This is a most valuable supplementary method in pneumothorax work. Serial radiograms afford most help in recognizing the position and extent of adhesions. It should be kept in mind, however, that even gross adhesions may not be obvious radiographically, and even when portrayed, their number or complexity cannot be gauged with accuracy. Therefore the most exact method of deciding the possibility of operation is direct examination of the pneumothorax cavity by the thoracoscope, a procedure which should be relatively painless and certainly without risk.

Division of adhesions, which demands a high degree of manual dexterity on the part of the operator, is carried out through an instrument like a cystoscope—the thoracoscope. The instrument is inserted through an intercostal space at a point which has been selected as most likely to give the best view of the adhesions, and one from which they will be more accessible for subsequent cutting. Division is performed slowly as close to the chest wall as possible with the electric cautery. Bleeding, when it occurs, is almost always from the parietal stump; it is controlled by light touches of a coagulating diathermy electrode or by a special hæmostat.

It is surprising how little upset accompanies or follows operation in experienced and careful hands. Subcutaneous emphysema occurs in a high percentage of cases. Some degree of pleural effusion is to be expected. It is usually slight and transient, but occasionally it persists, and in a few cases becomes purulent. The perfection of the technique has made hæmorrhage a rare occurrence.

**Phrenic Paralysis.**—Permanent paralysis of the diaphragm on one side can be produced by division at the root of the neck of the main and accessory phrenic nerve fibres, or evulsion of the entire nerve. Temporary paralysis,

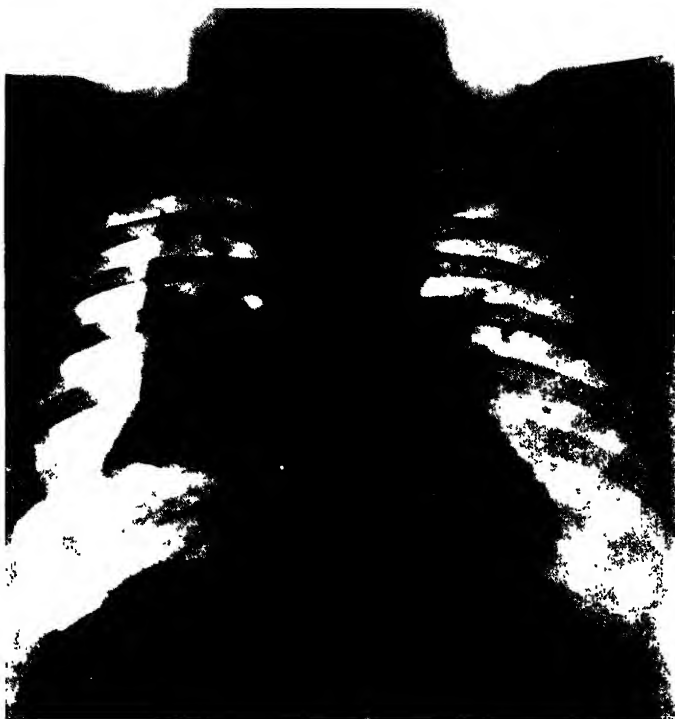


PLATE 5--Unsatisfactory artificial pneumothorax.  
Proper collapse is prevented by apical adhesions.



PLATE 6--Same case after intrapleural division of  
adhesions. A more satisfactory collapse has been  
achieved.

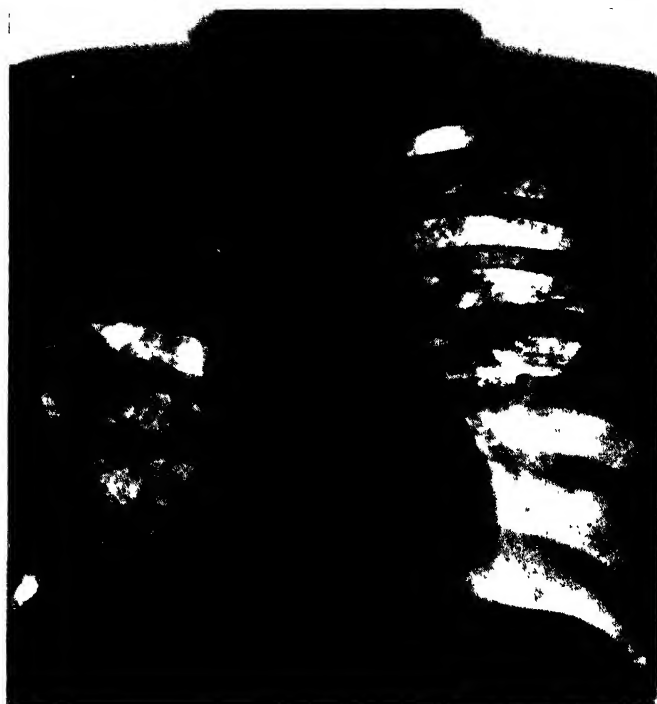


PLATE 7—Chronic pulmonary tuberculosis affecting right lung. Artificial pneumothorax had proved impossible owing to the presence of dense widespread adhesions.



PLATE 8—Same case six months after phrenicectomy. Note the considerable elevation of the diaphragm, and some improvement in the pulmonary lesions.

by crushing the nerve, lasts for six or more months and may meet the requirements of a case, because if the desired effect (usually fibrosis or closure of cavities) is not forthcoming within that period it can scarcely be expected later. The temporary operation as opposed to the permanent one is now employed more frequently. Operation is carried out under local anæsthesia without much discomfort and without untoward sequelæ. Phrenic paralysis results in elevation of the diaphragm with consequent reduction in lung volume, the combination of which favour healing throughout the lung, more especially those parts already undergoing fibrosis. The apical regions may derive benefit, but usually to a less extent than the middle and lower zones.

The indications for operation are numerous, but require exact specification if disappointing results are to be avoided. The prospect of success can be decided only by a studious consideration of the influences which delay resolution in the diseased parts of the lung. Haphazard operations are to be deprecated. The help of phrenicectomy is usually sought for unsuccessful pneumothorax cases. In acute cases it is seldom of assistance unless multiple soft-walled cavities are present. In more fibroid types, especially if there are cavities in the central and lower parts of the lung, great benefit, and sometimes cure, may be anticipated. The results are usually very disappointing in those common cases of stiff-walled cavities in the apical zones of the lung, and alternative methods of collapse are preferable.

Phrenic paralysis may be employed with value in combination with artificial pneumothorax, especially when diffuse adhesions are an obstacle to effective collapse, and also when additional collapse is required at the base of the lung and especially when a cavity persists in the apical segments of the lower lobe. As a preliminary to complete thoracoplasty, the temporary (not the permanent) paralysis may be helpful in that it may permit of a more circumscribed operation being effective.

Phrenic paralysis is sometimes indicated at the completion of treatment by artificial pneumothorax, so that the healed lung may not be exposed to undue strain as it re-expands. Troublesome symptoms, in otherwise untreatable cases, may be relieved by phrenic paralysis; *e.g.*, dry, spasmodic cough due to irritation of the diaphragm from the pull of an adherent lung can be abolished, and also the pain and dragging along the attachment of the diaphragm when there is old-standing basal pleurisy.

**Pneumoperitoneum.**—Pneumoperitoneum is often a valuable means of securing partial collapse of the lung when other methods have failed or are, for the time, not warranted. The diaphragm should have been paralysed previously to ensure the maximum elevation of the diaphragm after air is introduced into the peritoneal cavity.

The method is used most often to promote healing of disease in the lower lobe of the lung especially when cavitation is present and when pneumothorax alone is ineffective or unsecurable. In a number of instances quick and sound healing is obtained, but more often the disease, though improved, remains active. Pneumoperitoneum is of undoubted value as a means of temporary collapse before thoracoplasty: it may bring about considerable shrinkage of cavities in all zones of the lung, and a notable improvement in general health.

Some workers use pneumoperitoneum in preference to artificial pneumothorax in the initial stages of treatment of very active and acute disease in

the belief that massive pleural effusion will be less likely when the fitting time for pneumothorax arrives.

Pneumoperitoneum is induced and conducted on similar lines to pneumothorax: 500 c.c. of air are inserted into the upper abdomen at the induction, and additional quantities of air are introduced on alternate days until the optimum elevation of the diaphragm seems present. Finally, refills of about 1,000 c.c. of air are given weekly. The duration of treatment depends on the progress of the disease, but need not be so protracted as pneumothorax, especially as it can be re-established if required.

A certain amount of abdominal discomfort and shoulder pain on the unparalysed side may be complained of after the induction of pneumoperitoneum. This is not usually severe and yields to mild sedatives. Mediastinal emphysema and peritoneal effusion are occasional complications.

**Extrapleural Pneumothorax.**—When intrapleural pneumothorax proves impracticable on account of adhesions, and when the patient is unfit or unsuited for thoracoplasty, collapse may be obtained by stripping the parietal pleura with the upper lobe of the lung from the chest wall and mediastinum and maintaining the space so created by refills of air under pressure. The collapse obtained may be very satisfactory, but unfortunately complications such as hæmorrhage and infection are common and sometimes disastrous, so that the method has fallen into almost complete disuse.

**Thoracoplasty: Total and Subtotal (including Apicolysis).**—Thoracoplasty on the drastic lines once in vogue has given place to much more selective forms of rib resection and pneumolysis. Operation is usually considered only in chronic types of disease when less severe measures are impracticable on account of widespread pleural adhesions and the excessively indurated condition of the lung. It is specially valuable when there are multiple rigid-walled cavities, provided there is no active or uncontrolled disease in the other lung, and provided the circulatory system is not seriously impaired.

Thoracoplasty entails excision of lengths of bone from the posterior parts of the ribs as far back as (and usually including) the transverse processes of the vertebræ. The number of ribs and the amount of each removed varies according to the extent and character of the disease: it varies from four to ten ribs and should always include a liberal portion of the first and second. A manœuvre now commonly combined with thoracoplasty, and especially for upper lobe cavities, is extra-fascial stripping of the lung. It affords a free relaxation of the diseased parts and is usually successful in bringing about closure of stiff-walled cavities; indeed, extrapleural pneumothorax, once in vogue, was simply an elaboration of the same practice.

Considerable shock may follow extensive thoracoplasty; therefore it should be done in two or more stages. Cyclopropane, on account of its non-asphyxial properties, has proved the best anæsthetic, though local anæsthesia is favoured by some. The most upsetting complication after operation, especially the first stage, is atelectasis of the remaining uncollapsed part of the lung due to stagnation of bronchial secretions. When it occurs, attempts at relief by bronchoscopy should be promptly undertaken.

**Lung Resection.**—During the past few years the resection of a lobe or the entire lung has been extended to pulmonary tuberculosis when the disease is emphatically localized. Some striking successes have been secured, especially by lobectomy, when an indolent tuberculous process exists



PLATE 9—Chronic fibroid unilateral pulmonary tuberculosis. There is notable retraction of the mediastinal structures towards the diseased side.



PLATE 10—Same case two years after an extensive thoracoplasty. The patient is well and working.





within a shrunken lobe distal to a bronchial stricture. In general the results have been disappointing except in very specially selected cases.

**Drainage of Cavities (Monaldi).**—In selected cases intermittent suction drainage by catheter of an “inflation” cavity will bring about reduction in its size and sometimes total closure. Drainage may have to be continued for four to six months.

**Summary.**—Surgical methods should not be regarded either as a short cut to cure in pulmonary tuberculosis or as a final and desperate resort when all other forms of treatment have failed. It should be emphasized that they are not substitutes for the general methods of treatment. It is true that collapse therapy may bring about a spectacular improvement in an acute case and may remedy the otherwise permanent mechanical effects of chronic disease. Yet the various methods of collapse are merely accessories in a fight which is the concern of the resistance of the body, and general methods designed to increase this natural resistance are just as important in patients receiving collapse treatment as in those treated by conservative methods.

Artificial pneumothorax may shorten the duration of treatment by rest, and indeed this is one of the acknowledged advantages of the method. Too early resumption of activity, however, can mar what might otherwise have been a permanent success, and it is much better to “hasten slowly.”

When the disease has reached a stage that an operation such as thoracoplasty is needed, success is unlikely unless the general treatment of the patient receives careful consideration at the same time. Operation should be contemplated only when the maximum beneficial effect has accrued from general treatment. An extended period of rest in a sanatorium environment is imperative after the operation. Surgical interference is, indeed, only an incident in the course of treatment. It is usually six to nine months before the patient appreciates its full benefit. In well-chosen cases the outcome is very gratifying. Scoliosis and drooping of the shoulder girdle should not occur if physiotherapeutic measures are adopted during convalescence.

B. M. DICK.

### THE TREATMENT OF SYMPTOMS

**Cough.**—Cough is the most common symptom requiring treatment in pulmonary tuberculosis. A certain amount of coughing is often beneficial, especially in cases with cavitation, in order to free the air passages from secretions which are frequently toxic. A dry unproductive cough, however, serves no purpose and may be a factor preventing healing. Even when the cough is productive, it should not be so frequent as to exhaust the patient; it should not be allowed to disturb sleep unduly, nor should it cause vomiting after meals. It is better for secretions to be allowed to accumulate for some time and to be coughed up at intervals rather than to be coughed up in small quantities very frequently throughout the twenty-four hours.

It is often unnecessary and undesirable in the treatment of pulmonary tuberculosis to administer drugs to suppress the cough. Rest in fresh air which is free from dust is frequently all that is required to allay unnecessary coughing. Coughing is often a bad habit and patients can be trained to resist it. The cough may be persistent for a time, but if it is voluntarily

suppressed it tends to wear off; indeed, in a sanatorium for early cases one hears the visitors coughing a good deal more than the patients!

Patients who do not have large cavities in their lungs containing secretion can usually get their air passages cleared of sputum after waking in the morning, and need have no more coughing throughout the twenty-four hours. A warm alkaline drink on waking assists the loosening of such secretions and makes coughing easier.

Patients with pulmonary cavitation often find a certain position in bed in which the secretion drains most easily into their bronchial tubes. By assuming this position at certain times during the day their cavities are emptied more readily.

When the above simple measures fail, and the cough is excessive and disturbs sleep unduly, or when the cough is unproductive and useless, a sedative should be prescribed. Codeine is the drug of choice; it has a strongly depressant action on the cough centre and has few of the undesirable effects of the other alkaloids of opium apart from its constipating tendency. It may be given in tablet form in doses of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 32 mg.), or as syrup codeine phosphate in doses of 1 to  $1\frac{1}{2}$  teaspoonfuls. This dose may be given at night only, or three or four times in the twenty-four hours as required. In patients with large cavities and a severe cough which prevents sleep, a stronger sedative may be necessary. Mixtures containing morphine should, if possible, be avoided on account of their constipating effects and a linctus of heroin is preferable:

Ry	Heroin Hydrochlor.	.	.	.	.	gr. $\frac{1}{4}$ (4 mg.)
	Glycer.	.	.	.	.	M℥x (0.58 c.c.)
	Syr. Pic. Liq.	.	.	.	.	fl. dr. i (3.6 c.c.)

This should not be given sufficiently often to suppress the cough entirely during the night, as this will only result in increasing the toxæmia and will aggravate coughing the next day.

An "emetic" cough is a very troublesome complication which is often extremely resistant to treatment. When it is present, meals should be simple and frequent rather than few and large. The patient should keep very still for some time after eating and should not be allowed to talk. A codeine tablet or sedative linctus can be given before the meal. Severe cases, however, may continue to vomit all food taken in spite of these measures. Under such circumstances cocaine is the only drug likely to give relief: a 5 per cent. cocaine solution should be sprayed on the larynx before and after meals. Occasionally a pastille, such as is prescribed below, sucked immediately after a meal may be sufficient:

Ry	Menthol	.	.	.	.	gr. $\frac{1}{4}$ (16 mg.)
℥	Cocain. Hydrochlor.	.	.	.	.	gr. $\frac{1}{2}$ (3 mg.)
	Glycogelat. B.P.C.	.	.	.	.	q.s.

**Hæmoptysis.**—Of all the complications of pulmonary tuberculosis, hæmoptysis is probably the one which is most dreaded by the patient. Actually it is not usually a serious complication. Death as the immediate result is uncommon, and in the majority of cases hæmoptysis is not followed by an extension of the disease. Patients, therefore, should be encouraged to believe that hæmoptysis is not necessarily an untoward occurrence.

Slight streaking of the sputum with blood need not affect the general course of treatment in any way provided it is not accompanied by other signs of increased activity of the disease. There is no need to confine the patient to bed on this account alone.

When the hæmoptysis is rather more severe, the patient should be kept resting quietly in bed and should be encouraged in the hope that the bleeding will stop spontaneously. With moderate bleeding this is all the treatment which is necessary.

Profuse hæmoptysis is an indication for complete rest and careful nursing. An injection of  $\frac{1}{8}$  or  $\frac{1}{4}$  gr. (10 to 16 mg.) of morphia should be given to calm the patient's anxiety and restlessness, to render the breathing quiet and peaceful and to allay excessive cough. The physician has to steer a somewhat difficult course in respect of the subsequent administration of morphia. When given in large and frequent doses it will so inhibit the cough reflex that the blood may accumulate in the air passages and cause pulmonary atelectasis or aspiration pneumonia. Morphia should, therefore, be used to control undue cough, restlessness and apprehension, but not to the extent of rendering the patient semi-conscious with a completely suppressed cough reflex.

It is inadvisable to keep the patient flat in bed or to frighten him with the suggestion that the slightest movement will cause further bleeding. This will only add to the risk of atelectasis in the posterior parts of his lungs. He will be more comfortable moderately propped up in bed, and in this position it will be much easier for him to expel blood clots and sputum.

No solid food should be given for twenty-four hours after a severe hæmoptysis, and thereafter feeding should be started cautiously. The patient may drink fluids as he wishes, but these should not be hot.

The indications for blood transfusion are the same as for severe hæmorrhage in any other part of the body (see p. 474). The blood of all patients with profuse hæmoptysis should be typed and suitable blood procured and kept at hand.

Large numbers of drugs have been recommended from time to time for the treatment of tuberculous hæmoptysis. Emetin, pituitrin, congo-red, the nitrites, calcium, adrenaline, thromboplastin and many others have had their advocates. It would be irrational to suppose that any of them could influence a severe pulmonary hæmorrhage, and in our opinion they are quite worthless in practice.

The only form of active treatment likely to be successful is collapse of the affected lung by artificial pneumothorax if it can be effected (see p. 132). It is not always possible to say from which lung the hæmorrhage is occurring, but when this is known and the case is sufficiently serious, the feasibility of securing a rapid collapse of the lung as an emergency measure by a large initial injection of air up to 1,000 c.c. should always be considered. When a satisfactory collapse can be induced the bleeding is often dramatically arrested. When pneumothorax cannot be secured on account of pleural adhesions, crushing of the phrenic nerve followed by pneumoperitoneum may succeed in controlling hæmorrhage.

The after-treatment of a patient who has had a large pulmonary hæmorrhage is the same as for hæmorrhage in other parts of the body, and the anæmia should receive appropriate treatment with iron (see p. 470).

**Gastro-intestinal Symptoms.**—*A poor appetite and dyspeptic symptoms are*

common in untreated cases of pulmonary tuberculosis. They are often due to the general toxæmia which is present, and disappear with rest and fresh air treatment, which are much more efficacious in this respect than bitter tonics and stomachics. Irritation due to swallowed sputum is sometimes responsible for gastritis and enteritis, and for the much greater danger of tuberculous ulceration of the bowel. The patient must be impressed with the importance of expectorating all the sputum coughed up. Overfeeding is another common cause of dyspeptic symptoms, which should call for a review of the patient's diet (see p. 123), and when the symptoms are severe a day of virtual starvation may be beneficial.

*Hypochlorhydria and achlorhydria* are common in tuberculosis, as they are in all debilitating conditions. Where flatulent dyspepsia persists in spite of attention to the points already mentioned, a fractional test meal should be performed, and if achlorhydria is discovered, suitable treatment should be instituted (see p. 534).

*Diarrhœa* may be due to toxæmia, to tuberculous ulceration of the intestine or, occasionally, in advanced cases of long duration, to amyloid disease. When ulceration is present the benzidine test for occult blood is usually positive, and pus cells are present in the fæces. Because a patient is getting two or three loose stools a day it should not be concluded hastily that tuberculous ulceration of the intestines is present.

A dose of castor oil is the best treatment for simple diarrhœa, and the patient should be kept warm in bed. When symptoms persist the diet must be suitably altered. A low residue high vitamin diet should be given similar to that described for chronic dysentery (see p. 25). Milk and excessive fats may have to be omitted when the stools show that these are not well digested.

**Tuberculous Enteritis** is a very grave complication of pulmonary tuberculosis, and in our experience the results of treatment have been singularly unsatisfactory. Three therapeutic measures have been advocated recently, particularly from America, as specifics for the condition: (1) Exposure of the abdomen to ultra-violet radiation from the mercury vapour lamp; (2) the administration of massive doses of cod-liver oil and tomato juice; (3) the injection of oxygen into the peritoneal cavity. We have treated many patients by the two former methods without observing any beneficial results. We have had no experience of treatment by means of pneumo-peritoneum, but the published results are not convincing.

It is common for patients with tuberculous enteritis to be treated with a diet of milk and soft carbohydrate foods. This is a great mistake and renders the stools excessively loose and offensive. If a dry low residue high vitamin diet (see p. 578) is prescribed the stools cease to be offensive and the diarrhœa and flatulence are often considerably relieved. In advanced tuberculous enteritis associated with severe diarrhœa and abdominal pain, the patient should be fed at frequent intervals with small meals of steamed fish, clear soup, custard, jellies, crisp toast, and similar low residue food-stuffs, milk being avoided. For the pain, 10 minims (0.58 c.c.) tinct. opii should be given three times a day, the dosage being liberally increased as required, as there is no point in withholding sedative treatment from these unfortunate people.

Attempts at surgical resection of the ulcerated portion of bowel are almost invariably unsuccessful and frequently fatal.

**Pain.**—Severe pain in the chest in the course of pulmonary tuberculosis is usually due to pleurisy. In emaciated patients with advanced disease it may be caused by fracture of a rib by coughing, a complication which is more common than is supposed and frequently overlooked. Occasionally pain may be due to spontaneous pneumothorax (p. 743).

The treatment of pain from dry pleurisy or a fractured rib is the same. Broad strapping is applied over the affected side, each strip overlapping the other. The strips must extend 2 in. below the middle line both in front and behind, and should be firmly applied while the chest is fully collapsed in expiration. If this is insufficient to relieve the pain entirely, tab. codein. co. (B.P.) may be given. It is rarely necessary to administer morphia if the strapping has been correctly applied.

**Sweating.**—Sweating during sleep is the symptom which yields most rapidly to fresh air treatment. Even seriously ill patients rarely suffer from it if they are living under proper sanatorium conditions. When it occurs, therefore, it is usually an expression of the bad management of the case in respect of inadequate fresh air and excessive bedclothes. Exceptionally, however, "sleep sweating" persists in severely toxic patients in spite of proper physiological conditions. Such cases should be given a glass of milk and a biscuit immediately before going to sleep, and a similar feed may be left by their bedside to be taken should they wake during the night. The use of atropine or any other drug is valueless in the control of sweating.

Scrupulous cleanliness is essential for all tuberculous patients, especially fevered patients whose skin is too often covered with a sweat rash. This will be prevented if ambulant patients take frequent baths, which should not be too hot, and if they dry themselves vigorously afterwards with a rough towel. Patients who are confined to bed should be washed completely night and morning.

**Fever.**—Absolute rest in the fresh air is the best treatment for fever. It is easy to reduce the temperature by means of antipyretic drugs, but this procedure serves no useful purpose. Indeed, a helpful index of the progress of the disease is obscured, the tendency to sweating is increased and the temperature goes up again as soon as the drug is discontinued. If the fever is high and the patient is very uncomfortable, tepid sponging may afford relief.

## TUBERCULOUS PLEURISY WITH EFFUSION

When an effusion in the pleural cavity is suspected it is usual to make a confirmatory puncture. Some 15 c.c. of fluid should be removed for cytological and bacteriological examination. A clear sterile fluid containing a predominance of lymphocytes is almost certainly tuberculous in character. Tubercle bacilli can rarely be demonstrated in the effusion, and even its inoculation into a guinea-pig often gives negative results. The fact that it is sometimes impossible to prove the tuberculous nature of the effusion bacteriologically should not confound the diagnosis. The serious nature of so-called "idiopathic pleural effusions" is often insufficiently appreciated by the doctor, or its significance minimized owing to his dislike of revealing the underlying tuberculous nature of the condition. A large percentage of such cases develop obvious pulmonary tuberculosis subsequently, often due to insufficient care during the stage of effusion. Cases of tuberculous pleurisy

with effusion should therefore be treated in the same way as early cases of pulmonary tuberculosis, according to the criteria laid down on p. 116, and should not be allowed to pass out of medical care and supervision as soon as the effusion and immediate symptoms have subsided. The true nature of the condition should not be withheld from the patient or his relatives, and any illness or symptoms which may occur subsequently should be interpreted with due regard to the tuberculous history.

**Aspiration.**—In the majority of cases it is unnecessary and unwise to aspirate the effusion, apart from a few cubic centimetres for diagnostic purposes. If left alone the fluid will usually be absorbed spontaneously, and while it remains it probably serves a useful purpose by keeping the lung collapsed and at rest as in therapeutic pneumothorax. This rule of non-interference is frequently broken with disastrous results. Even in teaching hospitals it is all too common for enthusiastic house physicians to remove at one aspiration some 30 or 40 oz. of fluid from the pleural cavity. The lung is thereby forcibly re-expanded and any small subpleural focus of disease which it may contain is liable to be activated.

There are, however, certain occasions when careful aspiration of the fluid should be carried out. Occasionally the effusion is so large that serious dyspnoea or cardiac embarrassment may occur. Such pressure symptoms can be relieved by the removal of 15 to 20 oz. of fluid. Thereafter a slow, spontaneous absorption of the rest of the fluid may occur, since the greatly increased intrapleural pressure may itself have been sufficient to inhibit absorption by compression of the blood and lymph vessels. The "Rotunda" pattern of aspirating syringe (50 c.c.) with two-way or three-way connections, illustrated herewith, is one of the most satisfactory instruments for aspirations of pleural effusions. The needles should be of the trocar-cannula type to prevent injury to the lung.

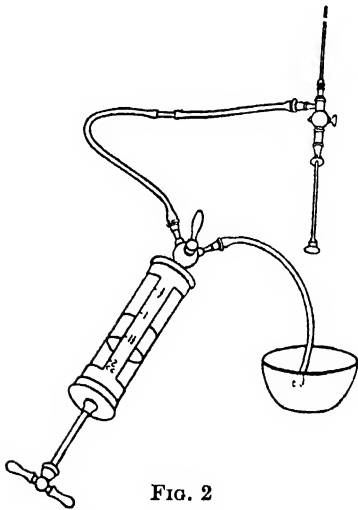


FIG. 2

Two-way Syringe used for Therapeutic Paracentesis. The trocar is shown partly withdrawn.

A second indication for the removal of an effusion is its persistence for an unusual length of time, as there is then danger of the underlying collapsed lung failing to re-expand satisfactorily. It is difficult to lay down hard-and-fast rules as to how long an effusion should be left before aspiration is undertaken, but if there are no signs of spontaneous reabsorption after five or six weeks, aspiration should be considered. No more than 15 oz. should be removed at a time, as it is most undesirable to produce a markedly negative intrapleural pressure. Such negative pressures may cause pain, distressing cough and œdema of the lung in addition to the risk of activating any tuberculous lesion within the lung.

Sometimes a patient experiences severe tightness or dragging in the chest after aspiration of an effusion, especially if a pneumothorax coexists (vacuum pain). Readjustment of the intrapleural pressure by inserting up to 50 c.c. of air usually brings prompt relief.

**Air Replacement.**—If active pulmonary tuberculosis in the underlying lung is suspected, or known to be present owing to the discovery of tubercle bacilli in the sputum, it is best to remove the pleural effusion and to replace it with air. To do this two needles are inserted into the pleural cavity, the one low down and connected with an aspirator, the other higher up in the axilla and connected with a pneumothorax apparatus. This arrangement allows the simultaneous withdrawal of fluid and its replacement with air, and by keeping the intrapleural pressure about zero, practically all the effusion can be withdrawn without the risk of causing coughing, pain or œdema of the lung. Further, the therapeutic collapse of the lung is maintained, and can be controlled at will. The amount of air required to replace the fluid is usually about half the volume of fluid withdrawn. The management of the patient after a successful air replacement is the same as for an ordinary case of artificial pneumothorax complicated by an effusion (see p. 135). Unfortunately effective collapse is frequently impossible owing to pleural adhesions.

## TUBERCULOSIS OF THE LARYNX

Tuberculosis of the larynx is a common complication of pulmonary tuberculosis. Apart from the rare condition of laryngeal lupus it is always secondary to pulmonary disease and, though it is usually associated with advanced pulmonary tuberculosis, it may occur in early and curable cases. Contrary to the usually accepted belief, early laryngeal tuberculosis is quite amenable to treatment—provided the underlying pulmonary condition is not too far advanced. Severe laryngeal ulceration (and especially if ulceration of the epiglottis co-exists) is exceedingly recalcitrant to treatment, and its presence greatly increases the gravity of the prognosis.

Thus examination of the larynx at regular intervals should never be omitted as a part of the routine management of all cases of pulmonary tuberculosis. Too often this examination is neglected unless symptoms of hoarseness or aphonia are present, by which time laryngeal ulceration may have occurred. Whenever possible the examination should be carried out by an expert, as early tuberculosis of the larynx is difficult to recognize.

Treatment of laryngeal tuberculosis cannot succeed unless the underlying pulmonary tuberculosis is treated concurrently. Since the laryngeal disease is caused by infected sputum, every effort should be made to reduce its quantity and the severity of the cough. Wherever it is feasible, artificial pneumothorax is the most useful measure at our disposal for this purpose. Tuberculosis of the larynx "per se" need not be a contraindication to thoracoplasty. If artificial pneumothorax is impracticable treatment with gold may be given a trial, as there is some evidence that such treatment has on occasion a distinct effect in reducing the quantity and infectivity of the sputum.

**Silence.**—Apart from attention to the underlying pulmonary condition, the sheet-anchor of treatment is rest, just as it is the primary consideration in the therapeutics of tuberculosis affecting any other organ in the body. The treatment of excessive cough by appropriate sedatives (see p. 140) is a factor of importance in this respect. Apart from this, rest for the larynx may be secured to a great extent by insisting that the patient should maintain complete silence. This Trappist rule may have to be continued for many months and demands considerable resolve on the part of the patient.



It is important, therefore, to explain fully at the outset that silence is of paramount importance and that serious consequences may ensue if the rule is broken. The patient should be provided with a pad on which to write his requirements, and a notice labelled "Silence," put over the bed, may be a reminder and may warn thoughtless people from asking the patient questions which might provoke a spontaneous reply.

Many authorities allow patients with tuberculosis of the larynx to whisper. When this is carefully done and the sounds are produced by the lips and mouth only, and spoken so that they do not carry for more than a few feet, it probably does not interfere to a significant extent with laryngeal rest. In our experience, however, patients who are allowed such latitude soon become careless about the manner of their whispering. The whisper becomes louder and louder until it ends as a stage whisper, which may be more of a strain on the larynx than ordinary speaking. We believe, therefore, that in curable cases speech in any form should be prohibited until the condition has subsided. Careful whispering should then be permitted, and only if the condition of the larynx has continued satisfactorily for a month should ordinary speaking be allowed. When the patient is allowed to speak after a long period of silence, he is usually unable to produce more than a hoarse whisper, as the vocal cords will not fully approximate. He should be assured that this is only temporary and that he will regain his voice in the course of time.

Smoking definitely aggravates tuberculosis of the larynx and should be forbidden.

**Cauterization.**—Apart from silence, the only treatment likely to prove of curative value in laryngeal tuberculosis is the cautious use of the galvanocautery. The procedure known as ignipuncture is used for reducing the œdema of the arytenoids when they become unduly swollen. The cautery at white heat is plunged into the turgid tissues at one or two points, and this may reduce the bulk of the swelling. The procedure is usually carried out through the direct laryngoscope, but can be accomplished with the aid of the ordinary laryngeal mirror.

The cautery may also be used to remove small granulations or nodules within the larynx itself or on the vocal cords, and may facilitate the healing of the local lesion. It is to be understood that such procedures should only be undertaken after expert advice has been procured, and should only be performed by those practised in the art of laryngoscopy. They are simply incidents in treatment and are not a substitute for the general treatment of the tuberculous condition, nor do they dispense with the necessity for silence on the part of the patient. Although by no means a formidable operation in the hands of experts (for it only involves a few minutes' treatment which should be painless), great damage can be done by injudicious and inexperienced interference.

**Palliative Treatment.**—Advanced tuberculosis of the larynx is a hopeless condition and calls only for palliative treatment. With ulceration, particularly of the epiglottis (which is very rarely involved in early disease), nerve endings are exposed and cause intense pain—especially on swallowing. The plight of such patients is very dreadful, and every effort must be made to relieve their sufferings. A 5 per cent. cocaine spray in aqueous solution, used before meals, is one of the most valuable palliative measures. Alternatively, the insufflation of orthocaine, a local anæsthetic powder, often gives

great relief. A suitable apparatus for introducing this preparation is a Leduc's insufflator. The powder is put upon a saucer and the patient inhales it through the apparatus. In extreme cases other methods can be tried, such as the superficial coagulation of the exposed ulcerated areas by diathermy, or the injection with alcohol of the superior laryngeal nerve. These are both specialized procedures and require the collaboration of an expert.

Many patients suffering from dysphagia due to ulceration of the epiglottis find it easier to take their meals while lying on their faces from a tray on their pillow. By raising the jaw and stretching the neck this manoeuvre tends to lift the epiglottis forward and thus to facilitate the passage of food past the ulcerated area.

We believe that such methods of active treatment as the direct application of ultra-violet light to the larynx and attempts at surgical interference on the diseased parts, are contraindicated. When pain is very severe, alcohol injection of the internal laryngeal nerves may afford relief.

D. M. DUNLOP.

## TUBERCULOSIS OF THE GENITO-URINARY TRACT

### RENAL TUBERCULOSIS

The kidney is the first part of the urinary tract to be involved in tuberculosis. It is not a primary and independent disease, but rather a local manifestation in a tuberculous patient, and is the result of blood-borne infection. Evidence or a history of previous or coexisting tuberculous disease is available in over 80 per cent. of cases. The common sources of infection are the lungs, bones and joints and lymph glands in the thorax or abdomen.

Routine and careful examination of the urine in subjects undergoing treatment for tuberculosis may reveal a tuberculous bacilluria. It is usually symptomless, though occasionally there is frequency of micturition. The presence of leucocytes and a few red blood corpuscles in the urine is invariable, and their detection should, therefore, suggest a prompt bacteriological examination. It is probably unnecessary to examine the urine for tubercle bacilli unless leucocytes are present. The underlying cause is an overt focus of disease in the cortex of the kidney which cannot be demonstrated at this stage by radiological investigation. Healing usually occurs, but in a few instances active and progressive disease of the kidney is manifest at a later date, and this possibility should be kept in view in the after-care of tuberculous subjects.

When renal tuberculosis is suspected, a very thorough examination should be carried out in order to confirm the diagnosis and to ascertain the extent of the disease. Intravenous pyelography is often of great value, but it cannot be relied on in every case because when the lesions are small the kidney may appear normal. Cystoscopy may be negative or may show a diminished bladder capacity, mild cystitis, miliary tubercles or ulceration. Finally, and especially when the diagnosis is in doubt, catheter pyelograms should be obtained; they give the clearest definition of structural changes in the kidney and ureter.

Early renal tuberculosis can be cured by general treatment alone, but this is only possible if the disease is in its initial stages, *i.e.*, when the

lesion is so small that it cannot be detected by pyelography and is only demonstrable by a few leucocytes, red cells and tubercle bacilli in the urine.

Once the disease has progressed beyond the early stage, and can be demonstrated by retrograde pyelography, spontaneous retrogression though not unknown is exceptional, and the question of nephrectomy has to be considered. It should be emphasized, however, that surgery will not benefit the patient fully until he has developed his resistance to tuberculosis, and this is best promoted by a period of residence in a sanatorium. It is remarkable how under sanatorium treatment the general health is improved, symptoms relieved and ulceration of the bladder diminished. Following constitutional treatment operation is more easily borne, convalescence more rapid and the risks of complications, such as generalization of the disease or affection of the remaining kidney, reduced. An uncontrolled lesion in the lungs is a definite contraindication to operation, for this focus will probably remain active and may be a source of infection to the remaining kidney. When severe disease affects both kidneys surgical interference is obviously contraindicated.

As in tuberculosis generally, the operative procedure is merely an incident in treatment. Many of the unsuccessful results of nephrectomy can be traced to insufficient post-operative care. Responsibility does not end with the immediate recovery of the patient from the operation. A period of from three to six months' convalescence in a sanatorium, or under sanatorium conditions at home, should be enforced, no matter how well the patient may appear.

Following operation the bladder, if it has been affected, may recover with remarkable rapidity, but not infrequently a considerable time (even years) may elapse before this takes place. Unfortunately, there are many cases in which ulceration of the bladder persists and leads to great contraction of its walls. In these cases pain and frequency of micturition may be very distressing. Little relief is secured by local treatment, and generally resort must be made to increasing doses of anodyne drugs. Occasionally transplantation of the ureter may be feasible.

A review of statistics suggests that nephrectomy for tuberculosis of the kidney results in cure in about 60 per cent. of cases. One of the chief objects of nephrectomy is to safeguard the bladder from extension of disease, and when it is affected to facilitate its healing.

### TUBERCULOSIS OF THE GENITAL TRACT

**Genital Tuberculosis in the Male.**—This may occur as an isolated manifestation, but in approximately 50 per cent. of cases it is associated with tuberculosis of the kidney. This fact must be kept in mind when treatment of either system is considered and a careful investigation of the whole genito-urinary tract should be made. The testicle with its epididymis is the only secretory part of the male genital system which is exposed to direct examination, but on account of the tubular connections of the components of the tract tuberculosis is rarely confined to one structure. The epididymis is most frequently involved, but in the majority of cases the prostate and seminal vesicles are coincidentally diseased. The primary focus may be in the prostate and involvement of the epididymis may be a later manifestation. The tendency to infection of the second epididymis at a later date is well

known. These facts are of importance in treatment, and surgical interference should never be resorted to hastily. The remarks with regard to the value of a preliminary period of conservative treatment in renal tuberculosis (see p. 148) apply with equal and even greater force, and rest in bed under good conditions of hygiene and diet, with the affected testis supported by a suspensory bandage or pad, should be the first measures employed. With this treatment the swelling may gradually subside and the enlarged nodular epididymis may become small and fibrous. More commonly caseation and abscess formation result and it is at this stage that opinion is divided on the question of surgical interference. It is the authors' opinion, based on their experience, that these localized swellings should be left until skin involvement takes place. The pus should then be evacuated by incision. A sinus invariably forms but usually heals within a few months after extrusion of the caseous débris. The body of the testicle is seldom involved. If, as rarely happens, the sinus does not heal and is obviously related to persisting caseous masses, the question of excision of the destroyed epididymis and the sinus track must be considered. If the body of the testis becomes diseased, orchidectomy should be performed, but the practice of early removal of the testicle is to be deplored. It does not prevent the involvement of the other organ and may, in fact, conduce to it. Peripheral surgery can have no effect on the pelvic components of the tract, and the radical operation of removal of the whole genital tract meets with little favour.

In those combined cases where there is ulcerative disease of one kidney, that organ should be dealt with as an isolated problem. If it is extensively diseased its removal will not only protect the remainder of the urinary tract but will probably have a beneficial effect on the patient's power of resistance to disease elsewhere.

If there is no associated pulmonary tuberculosis, benefit, particularly with regard to the healing of sinuses, may be obtained from ultra-violet irradiation (see p. 409) and by a carefully administered course of tuberculin (for Technique see p. 152).

**Genital Tuberculosis in the Female.**—This is usually thought to be much less common than in the male, but it is probable that it occurs with greater frequency than has hitherto been realized. The fallopian tubes are the parts most frequently involved, but in a majority of cases there is coincident disease of the endometrium. The disease in both is often latent and symptomless and in this state is responsible for about 5 per cent. of all cases of female sterility. The ovary shows the same resistance to infection as does the testis.

In women who have clinical symptoms there is usually a detectable swelling of one or both tubes, and when this stage is reached the disease tends to spread widely throughout the pelvis with ultimate abscess formation in the tubes and pelvic cellular tissues. Spread to the abdomen is common and is the explanation of many cases of abdominal tuberculosis in young women.

In the latent stage the condition can only be diagnosed by endometrial biopsy, and it is as a rule discovered during the routine investigation of sterility. These patients are usually in good health and may not show evidence of active tuberculosis, and the question of treatment is a difficult one. The sterility, which in the majority is due to tubal occlusion, is likely to be permanent, but a period of general treatment is a wise recommendation.

Operation is now reserved for young women with a large tuberculous pyosalpinx where secondary infection might lead to disastrous results. In most cases of chronic tuberculous salpingitis the diagnosis remains presumptive and treatment is carried out on general lines, usually with great benefit. In a small group the symptoms of pain and irregular menstruation become increasingly worse and the patient becomes bedridden and miserable. In such cases radical operation is to be recommended, although the dangers of fæcal fistulæ and miliary spread are by no means negligible. In symptomless tuberculous endometritis a period of general treatment, as already stated, should be recommended, as in over 90 per cent. of cases the fallopian tube is also involved.

## GLANDULAR TUBERCULOSIS

Any group of lymph glands may be the seat of tuberculous infection. The mucous surfaces of the pharynx, bronchi and the small intestine are the usual portals of entry. Accordingly, the cervical, tracheobronchial and mesenteric systems are most commonly involved. The general treatment is on the lines already outlined (see p. 116) and the strictness of the regimen imposed should be governed by the presence or absence of constitutional signs and symptoms.

### TUBERCULOSIS OF THE MEDIASTINAL GLANDS

When tuberculous infection becomes established in a person previously free from tuberculosis—this is known as the primary tuberculous infection—a definite pathological pattern is followed. A small area of disease is formed at the point of establishment and the infection passes quickly into the lymphatics and reaches the nearest group of glands. The area of disease, the so-called primary focus, usually heals quickly. The disease in the glands persists for a longer period but it also heals in the majority of cases. The glands bear the brunt of all primary infections, and as 80 per cent. of these take place by inhalation, disease of glands in the lung roots is not uncommon. The glands involved are the hilar groups which surround the main bronchi, but these glands have connections with glands in the mediastinum and through them with supraclavicular glands. Tuberculosis of mediastinal glands thus implies a condition which is secondary to a primary lung infection, but the term is a useful one to indicate the intrathoracic glandular swelling which is the prominent part of that condition. The anatomical connection with supraclavicular glands is important. Swelling of that group is not true cervical gland tuberculosis but an extension of deeply seated intrathoracic disease and as such is unsuitable for surgery.

Most primary infections are trivial and pass unnoticed, and it is the exceptional infection which causes sufficient disturbance of health to demand investigation. Then one may find, usually by X-ray examination, a small area of tuberculous broncho-pneumonia and associated swelling of glands in the lung root. These infections after early childhood tend to heal quickly and require nothing more than the general measures of rest, proper feeding and care already described (p. 116). Treatment should be continued until symptoms have disappeared and health is restored. If the radiographical shadows have been extensive, treatment should be controlled by periodical

X-ray examination, for many children appear to regain health before the disease is actually healed.

Occasionally diseased glands may cause partial or complete bronchial obstruction. They do this by pressure on, or more commonly by caseous erosion of, a bronchus, and collapse of a lobe or lung segment is a not uncommon accompaniment of the condition. Mild obstructive symptoms, such as stridor and spasmodic cough, usually subside with rest and general treatment and these should be given a fair trial; but if the symptoms persist or become worse, bronchoscopy should be performed. Many of these cases have been found to be due to partial blockage of a bronchus by tuberculous granulations or caseous gland masses and the symptoms disappear after removal of the obstructing material. The value of such a procedure in preventing permanent collapse and subsequent bronchiectasis is obvious.

Children suffering from active tuberculosis of any type are in poor general health and most are benefited by cod-liver oil or one of the fat-soluble vitamin concentrates. Some have a secondary anæmia and are benefited by iron.

### TUBERCULOSIS OF THE CERVICAL GLANDS

The primary tuberculous infection has been discussed (p. 150). In the majority of cases it enters the body by inhalation and gives rise to a focus in the lung. In a minority the infection, either by inhalation from human sources or by ingestion of infected milk, is arrested in the lymphoid tissue of the tonsil or pharynx and passes to the group of lymphatic glands which drains them. These glands form part of the upper deep cervical chain and the tonsillar glands which take the main drainage lie slightly below and behind the angle of the lower jaw. It is these glands which enlarge and form the familiar swelling which is typical of the condition. In some cases the enlargement is gradual. In many it appears suddenly. Neither mode of onset gives any indication of the subsequent course of the infection, but on the whole glands which swell suddenly caseate quickly. The swelling is usually well localized, but occasionally it is bilateral and glands of the chain below and of the upper part of the posterior chain may be affected. Statistics show that in about 50 per cent. of cases of upper cervical gland tuberculosis the tonsils are tuberculous.

In many cases the swelling, particularly if the enlargement has been gradual, tends to regress and in time may be represented by no more than a few palpable fibrous nodes. In other cases the gland mass undergoes caseation and abscess formation, and the abscesses, initially confined by the gland capsule, perforate into the tissues of the neck and form a superficial abscess swelling. The track of these abscesses is sinuous, and when they discharge drainage is imperfect. Chronic sinuses may persist and give rise to a tuberculous infection of the surrounding skin (scrofuloderma). In other cases again the glands caseate but do not soften immediately. Glands of this type persist as large, firm, more or less stationary masses. These facts are important from the point of view of treatment.

It is unusual to find other associated tuberculous lesions. The condition to that extent is not serious, but treatment requires judgment. There need be no controversy about medical or surgical methods. General medical

treatment is always desirable, and in the type of swelling which shows a regressive tendency may be all that is necessary. An initial period of observation on these lines should be the first line of approach and the state of the tonsils should always be assessed. If they appear to be healthy they should be left alone. If they are unhealthy they should be removed, but the time of removal depends upon the state of the glands. If the glands are not obviously softening, and if the condition of the patient is good, tonsillectomy should be performed as a preliminary measure of treatment. If the glands are softening, or the state of the patient is poor, the tonsils should be left for later consideration.

Glands which have softened will in time form superficial abscesses, and very often a patient is seen for the first time in that condition. Aspiration of these abscesses is unsatisfactory. The pus is only partly liquid and contains masses of caseous material which block the aspirating needle, and persisting attempts merely lead to sinus formation along the needle tracks. It is better to evacuate the abscess by a small incision made in the line of a natural skin crease and to express the contents gently with a gauze swab. The lips of the small wound tend to close, and to ensure proper drainage it may be necessary to separate them daily with sinus forceps, paying careful attention to asepsis. If destruction of the gland has been complete the sinus will heal and cure result. More often the wound heals but a firm, enlarged, partly caseous gland remains. If this gland is left it will repeat the process of softening and abscess formation. When the incision wound is healed and the scar is healthy it should be removed.

Softening of glands which are under observation is a sign for immediate surgical removal while the pus is still within the gland capsule; and glands which remain enlarged and unchanged over periods of months are always caseous and should be excised.

A type seldom seen nowadays is diffuse bilateral upper neck gland enlargement extending down the neck and often reaching the supraclavicular regions. This type is unsuitable for surgery and demands patient medical treatment. Softening of individual glands may take place over long periods and requires treatment on the lines already indicated. In time quite extensive involution of swellings below the main tonsillar masses may take place and the surgical removal of these masses, now comparatively isolated, may be justified.

It should be remembered that while complications of tuberculous cervical glands are few they do occur, and a period of general medical treatment (p. 116) is always desirable. When the gland involvement is extensive and when suppuration has taken place it is essential, and it should be continued until the gland condition is healed and the general health is obviously restored. Open air treatment is always helpful, and treatment by natural sunlight or ultra-violet light from artificial sources (p. 409) is of undoubted benefit. When natural sunlight is used, precaution must be taken against overheating.

**Tuberculin.**—The action of tuberculin has been discussed (p. 128) and the product is well worth a trial, particularly in that fortunately disappearing type of diffuse glandular involvement with sinuses and scrofuloderma. The only exact method of administration is by injection and it is necessary to start with small doses. A preliminary Mantoux test, performed by the intradermal injection of 0.1 c.c. of a 1-10,000 solution of Koch's old tuberculin

or of 0.0002 mg. of P.P.D. (purified protein derivative supplied in powder with a diluent solution), will enable one to form an estimate of the patient's sensitivity; but as it is old tuberculin which is used in treatment it is easier to dispense with a preliminary Mantoux test and to start with a very small dose of that preparation and to increase the dose according to the resulting reaction.

Old tuberculin is supplied undiluted in 1 c.c. phials, and from one phial a series of dilutions is made. The diluent is physiological saline solution containing 0.5 per cent. phenol. 9 c.c. of the diluent are placed in each of five 10 c.c. wide-mouthed glass-stoppered bottles. 1 c.c. of pure tuberculin is placed in the first bottle, giving a dilution of 1-10, and 1 c.c. of this dilution is transferred to the second bottle, making a dilution of 1-100. This is repeated throughout the series and a dilution of 1-100,000 is finally reached. The initial dose by subcutaneous injection is 0.1 c.c. of this dilution. A reaction manifests itself by induration at the site of injection, by a rise of temperature, by a feeling of tightness in, or actual swelling of, the glands, and by headache and malaise. The most sensitive reaction, and that most easily determined, is local induration and redness at the site of injection. If no reaction occurs a second injection of 0.2 c.c. of the same dilution is given a week later and the dose is increased weekly by 0.2 c.c. When 1 c.c. of the 1-100,000 dilution is reached, 0.2 c.c. of the next dilution (1-10,000) is given. Even in patients with a considerable degree of sensitivity it is unusual to get reactions with the early doses, and when the tolerance dose is reached the reaction is likely to be mild. When this dose is reached it should be repeated once or twice until it ceases to cause a reaction. The scale of increase is then resumed. If the reaction is of any intensity the injections should be stopped until it has subsided. When they are resumed, the dose should be lower and the weekly scale of increase should not exceed 0.1 c.c. In this way patients can usually be carried on to the higher strengths and the course should end with 1 c.c. of the 1-10 dilution repeated several times. Many sensitive patients never reach this dose and their maximum should be that dose which gives a repeated mild reaction. Apart from obvious reactions, if there is any indication that the course of the illness or the patient's general condition is being affected adversely the injections should be stopped.

Tuberculin is not stable in dilution, and even when stored in the dark and in a cool place its potency cannot be guaranteed after four weeks. It is that fact, coupled with the facility rather than any virtue of the method, which led to the administration of tuberculin by inunction, the so-called percutaneous method. Tuberculin ointment consists of old tuberculin in a lanolin base and is supplied in strengths varying from 10 to 50 per cent. A piece of the size of a split pea is rubbed for five minutes with a glass rod into the carefully cleansed skin of the chest or abdomen. The inunctions are made at weekly intervals and it is wise to start with the 10 per cent. strength. A local reaction consists of a papular or papulo-vesicular rash at the site of inunction and this forms the guide to the strength which should be used. It is very unusual to get general reactions with this method, but mild focal reactions are not uncommon. Fresh areas of skin are used each week to allow complete subsidence of previous reactions. This method of giving tuberculin is safe, and although the amount absorbed is unknown it is effective. It is the method recommended for children.



### TUBERCULOSIS OF THE MESENTERIC LYMPH GLANDS

Enlargement and caseation of the mesenteric glands is a very common outcome of milk-borne infection in childhood. It may be, and commonly is, a primary source of infection in the body. The glands most commonly affected are those of the ilcocæcal region. They may reach such bulk as to be readily palpable through the abdominal wall. Gradual healing is the rule and calcification the usual dénouement. In rare instances a gland may soften and rupture into the peritoneal cavity, giving rise to acute—though not necessarily fatal—peritonitis. Inflammatory adhesions quite frequently occur and are one of the common causes of acute intestinal obstruction in adults.

The effects of the disease may be so mild that it is not suspected, but in young children it may be responsible for chronic digestive upsets, malnutrition and frequent and obscure febrile attacks. Sometimes there are more acute attacks, like appendicitis, and, unless the glands are palpable, differentiation is practically impossible. In practice it is wiser to ignore the possibility of tuberculous glands being the source of acute pain in the lower abdomen lest an early opportunity be lost of removing a diseased appendix. The diagnosis of appendicitis will usually prove more acceptable to anxious parents than that of tuberculosis.

When the diagnosis of tuberculosis of the mesenteric glands can be established, treatment should be on general lines to increase resistance. In very young children the disease may be the source of a more generalized infection, and this possibility should be kept in view when any subsequent illness arises. However, in the majority the infection remains localized, the glands become calcareous and no permanent ill-effect remains.

In the course of operations for appendicitis discovery of caseous mesenteric glands is very common. It is both unnecessary and unwise to interfere with them unless rupture seems imminent. It may be more prudent to withhold knowledge of the incidental discovery from nervous parents, as an uneventful recovery may be anticipated. When constitutional symptoms are present, however, general treatment must be instituted along the lines already mentioned, including a course of heliotherapy and tuberculin, provided the symptoms are not very acute.

### PERITONEAL TUBERCULOSIS

The treatment of the other manifestations of abdominal tuberculosis such as tuberculous enteritis and tuberculosis of the mesenteric glands has been discussed on pp. 142, 154; in addition, tuberculosis may involve the peritoneum; sometimes the various lesions are combined in different degrees. The disease is commonest in childhood, but not confined to that period.

In the peritoneum the disease may assume a miliary form—blood borne, or from an active glandular or other lesion in the abdomen. In such cases the general illness may overshadow the abdominal features. It usually progresses to a fatal issue, but when the disease is confined to the abdomen it may be survived. More often the infection is of a chronic nature and is manifest pathologically by (1) multiple and diffuse sub-peritoneal infiltra-

tions and a profuse serous effusion, or (2) by an accumulation of gelatinous or caseous exudate upon or between mesenteric and intestinal surfaces—which may become confluent in an inextricable mass. Both types may be associated with a severe and continued systemic disturbance. In the early years of life the outlook is grave, but in older children the prognosis is very favourable, especially in the ascitic type.

In all cases a sanatorium regimen should be enforced. A very rapid and striking improvement is usually witnessed, as evidenced by a diminution of the systemic intoxication and of the abdominal swelling from absorption of the effusion, though disappearance of the masses within the peritoneum is more gradual. The sanatorium regimen may, with advantage, be supplemented by heliotherapy when the disease has reached a stage of comparative quiescence. The once common practice of evacuating the effusion by operation should be abandoned; it deals with a beneficent expression of the disease and does not influence the underlying and still active sources of toxæmia. Occasionally the ascites may reach such dimensions as to cause serious embarrassment, and relief by tapping may be required (see p. 944).

The exudative form of infection follows a more protracted course. The prognosis is less favourable than in the ascitic form because cold abscesses may occur with eruption at the umbilicus, commonly causing a fæcal fistula. Further, when healing occurs the diffuse adhesion of bowel and mesenteries entails a continued menace of obstruction. It is remarkable, however, how seldom the obstruction reaches such a degree as to demand relief by surgery. After reaching a certain climax the obstruction usually relieves itself spontaneously. Should operation become necessary, the universal adhesions may render the operative manœuvres more than usually difficult.

## TUBERCULOSIS OF THE SKIN

Tuberculous infection of the skin causes a chronic inflammation whose features vary according to the extent of the infection and the route by which it has reached the skin. Thus, *lupus vulgaris* results from a blood stream infection or from extension from an adjacent diseased mucous membrane, *scrofuloderma* from caseating underlying tuberculous glands and *tuberculosis verrucosa cutis* from direct infection through an abrasion or wound. Treatment is the same for all types, with minor modifications to meet conditions in different areas.

Treatment has been to a large extent revolutionized by the recent introduction of calciferol, and this is now the primary treatment of choice. With very few exceptions, such as for small persisting nodules, caustics are seldom employed, and, on account of the danger of subsequent malignant transformation, X-ray treatment is not now used.

Calciferol (vitamin D<sub>2</sub>) is administered by mouth in the form of one of the high-potency Ostelin preparations which are issued as tablets containing 50,000 units of the vitamin. It is usual to start with a daily dose of 100,000 units and if, after a week, there are no signs of intolerance to increase the dose to 150,000 units. If symptoms of intolerance occur with a dose of 100,000, a daily dose of 50,000 should be tried. The tolerated dose should be maintained as long as improvement continues and may be given with safety for a period of six or more months. In cases which respond favour-

ably, improvement is usually progressive during the first nine months. About twenty per cent. of patients show symptoms of intolerance in the form of nausea, anorexia, tiredness and, occasionally, vomiting. These call for discontinuance of the drug and its resumption in a smaller dose when the symptoms have subsided. If intolerance persists, treatment must be abandoned. In all cases when improvement is well established the dose, after a few months, should be reduced, but the maximum tolerated dose up to 150,000 units a day should always be used in the early stages of treatment. Aggravation of the disease must be expected in the early weeks of treatment, but this in itself does not demand a reduction of the dose.

With doses of this size toxic damage (calcification of arteries) is unlikely to result, but it is advisable to make monthly estimations of the serum calcium. The action of calciferol on the serum calcium is irregular and bears no relation to clinical improvement, but if the level rises persistently above 12 mg. per cent. the drug should be discontinued until the calcium has fallen to a normal level (9 to 11 mg.).

Treatment on these lines leads to cure in about twenty per cent. of cases and to considerable improvement in a further fifty per cent. These results are no better than those of light treatment, but they are achieved in less than a third of the time and at considerably less expense and inconvenience.

Treatment by a combination of irradiation by the Finsen-Lomholt lamp and general irradiation by the carbon-arc lamp is still favoured by many dermatologists and is sometimes used in conjunction with calciferol treatment, although there is no evidence that a combination of the two methods yields better results than the light or calciferol alone.

The Finsen-Lomholt lamp concentrates the ultra-violet portion of a carbon-arc light spectrum while at the same time removing the visible light and the infra-red rays. The concentrated beam of ultra-violet rays is applied by applicators which exercise direct compression of the diseased area (to render it avascular), and small areas only can be dealt with at a time. An inflammatory reaction is produced, and this is associated with disintegration of the tuberculous foci and their replacement by fibrous tissue. Applications are repeated until the disease appears to be healed. General irradiation with a carbon-arc lamp can be used in conjunction with this treatment, and almost all patients benefit from carbon-arc irradiation alone. General irradiation is carried out several times weekly for a period of months.

Tuberculous skin lesions can often be improved greatly by a course of tuberculin injections (for technique see p. 152) which may usefully supplement treatment by light.

It should be impressed on patients suffering from lupus that regular attendance for treatment is essential and that they must keep in touch with their doctor for two years after apparent cure. Thereafter they should report immediately if there is any sign of recurrence.

The scarring and facial deformity resulting from extensive lupus can often be improved by plastic surgery using free and pedicled skin grafts supplemented, in the case of the nose, by cartilage inlays.

C. CAMERON.

# COMMON DISEASES OF THE SKIN

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## INTRODUCTION

**A**LARGE proportion of the skin diseases met with in general practice lend themselves more readily to treatment than the common disorders of other organs. Disease of the skin can be recognized as soon as it develops, remedies can be applied directly to the affected area and response to treatment can be ascertained by direct observation. In spite of such ideal conditions the cure of skin diseases, and by that is meant the complete disappearance of an eruption but not freedom from recurrence, is often exceedingly slow. The tendency for skin diseases to recur is notorious.

## CAUSE OF DISEASE AND RESPONSE TO TREATMENT

Skin eruptions and alterations in cutaneous function and structure can be produced by the action of noxious substances which reach the skin either from the outside or from within via the blood stream. It is the possibility of this direct external contact with irritants and poisons which renders the skin vulnerable to types of injury which are unknown in other organs.

Since disease of the skin may be produced by internal causes, the skin may suffer in conjunction with disorders of the internal organs. In these circumstances the visceral disease usually gives rise to the more serious manifestations and the skin eruption is regarded as of less importance. In addition to such eruptions there exist a number of skin diseases obviously due to some internal factor which appears to poison the skin alone. Here treatment is directed against the cause if this is known, or is governed by the principle of free elimination and the administration of some drug which experience has shown to be beneficial.

One important point must be noted in connection with skin disease, namely, that the interference with skin function which is bound to result from an extensive eruption does not necessarily produce any grave systemic symptoms or upset in general health such as accompanies the derangement of function associated with disease of other organs. Nevertheless, extensive destruction of the skin surface may prove fatal. Modification of function plays a great part in the treatment of disease of certain organs other than the skin, but physiological variation in the skin can only be produced to a limited extent, and the employment of methods calculated to produce such changes is not rewarded with much success in the treatment of skin diseases.

From what has been said it may be gathered that the treatment of skin disease solely by internal methods, while often desirable on theoretical grounds, is not entirely satisfactory from the practical point of view. With the exception of syphilis and leishmaniasis there exists no specific internal cure for any skin disease. Nevertheless, internal measures are valuable aids in a number of conditions, but, unless combined with external methods of treatment, they are, generally speaking, insufficient. In some cases a combination of both external and internal treatment is essential.

Before discussing separately the treatment of the common skin diseases, it will be an advantage first of all to give a detailed description of the technique employed in the application of external remedies, for this is a subject of particular importance.

It may be said without fear of contradiction that but for external treatment few skin diseases would ever be cured. Yet criticism is still levelled against dermatologists by some internists because of this dependence on external remedies. This is hard to understand, for if the drug employed acts unchanged on the diseased organ, it would seem to matter little whether it reaches the organ via the blood stream or by direct application. Moreover, direct application ensures that the drug reaches the cells of the organ to be treated more quickly, more certainly, and in a more controlled concentration than is possible through the blood stream.

A large variety of chemical substances are applied externally in the treatment of skin diseases and each one of them may be observed to have an almost specific healing action in individual examples of each disease. Certain chemicals or groups of chemicals are indicated in the majority of cases in each disease group, but there is invariably a small number of patients whose skins will not tolerate the applications which are generally employed. Again, different chemicals are suited to the different phases of the same disease. Two types of cutaneous intolerance to chemical applications may therefore be revealed in the treatment of any one skin disease; firstly, a general cutaneous idiosyncrasy to the chemical applied, and secondly, a temporary intolerance dependent on the phase through which the disease is passing. Both types may depend to some extent on the concentration of the drug applied, and by reducing the concentration the intolerance may disappear. On the other hand, the idiosyncrasy may be towards the chemical irrespective of its concentration. Intolerance of the first type may be considered an example of individual variation, whereas in the second type it constitutes a true idiosyncrasy. No matter what may be the nature of the intolerance it constitutes an obstacle to treatment, for it may be exhibited to such universally employed substances as fats and mineral oils.

Only general statements can be made regarding the pharmacological actions of the numerous remedies applied externally in the treatment of skin diseases. Some are absorbent; some, by evaporation, have a cooling and decongestive action; alteration of the fluid content of the epidermal cells may be produced by wet dressings; osmotic effects, surface tension changes and alterations in electrical conditions at cell surfaces may be induced; epidermal growth may be stimulated or inhibited. Such actions are bound to occur, but the effect of a given drug cannot definitely be ascribed to any one of them. All that can be said with certainty about the common chemical applications is that they have antiseptic properties, and in high concentrations act to a greater or less extent as irritants, and even cause the death of living cells. Their successful manipulation depends not on a knowledge of their pharmacological action but on a knowledge of skin disease in each and every one of its phases, an experience of the effect of a chemical substance on any one of these many phases, and an appreciation of cutaneous idiosyncrasy.

Since our accurate knowledge of the pharmacological action of the substances applied externally to the skin is so limited it will serve no purpose

to tabulate them in a list which could not be arranged in any significant classification. Their consideration, both as to method and strength of application, will therefore be deferred to the discussion of the treatment of individual diseases. In the majority of cases, however, the chemical substance is applied to the skin diluted in a vehicle, and the type of vehicle may profoundly influence the result obtained. It will, therefore, be advantageous to give a detailed description of such vehicles and the technique of their application, in order to avoid subsequent repetition.

The response of any skin disease to a suitable form of treatment depends on the efficiency with which it is carried out, and on the facilities available for doing so. It is not infrequently noted that a treatment which is eminently successful in hospital has proved of little value when carried out by the patient in his home. Skin applications are unfortunately expensive, and as a result treatment is sometimes unsatisfactory and prolonged because of false economy.

### LOCAL TREATMENT

Generally speaking, the use of soap and water is indicated in the treatment of all skin diseases for general cleanliness, and for assisting the removal of surface therapeutic applications and the products of the disease, such as crusting and scaling. Washing may cause a temporary increase in itching and burning, but this can be ignored in the majority of cases as it is generally transient. Occasionally, however, very sensitive inflamed skins will not tolerate the use of soap and water because the reaction which is produced does not subside rapidly, and the condition is aggravated. In such cases cleansing has to be carried out exclusively with olive oil, or peach kernel oil. It may also be necessary to use these oils prior to washing with soap and water in order to soften crusts or therapeutic agents which have been applied to the skin. Occasionally patients complain of a feeling of irritation and dryness after the application of olive oil, but this is rarely a serious drawback to its use.

**Baths** may be given in all skin diseases but may on occasion cause irritation in the same way as when soap and water is used for washing purposes. The temperature of the bath should not be more than 100° F., and a patient may soak in it for fifteen to twenty minutes. A number of drugs may be added to the bath, but it is very doubtful if such medicated baths have any real value, although patients with an extensively inflamed skin may find a starch bath more comfortable than an ordinary one. The following are the common drugs which may be added to a bath of approximately 40 gals.

**Starch bath:**  $\frac{1}{2}$  lb. of starch is first mixed with cold water in a basin to make a paste, and the bath is filled by allowing the hot water to run into the basin and overflow from it into the bath.

**Potassium permanganate bath:** Potassium permanganate crystals are added in sufficient quantity to make the water a bright pink colour, and the patient is immersed for ten minutes before soap is used.

**Bran bath:** 4 lbs. of bran contained in a muslin bag are placed in the bath, which is then filled by allowing the tap to run on to the bag.

**Sulphur bath:** 2 to 4 oz. of potassa sulphurata are put in the bath prior to filling.

The cleaning of the bath contaminated by medicaments added to the

water, or by pastes or exudations from the patient's skin, is a matter of importance. Sulphur, potassium permanganate, tar, chrysarobin, silver nitrate and the aniline dyes will stain a bath if it is not cleaned immediately and thoroughly after use. For a greasy bath, Vim, Brooke's soap or paraffin may be used; for chrysarobin, a mixture of paraffin and bath-brick; for the aniline dyes, turpentine or methylated spirit.

**Powders.**—For ordinary purposes starch, talc or kaolin, used either singly or mixed in equal parts, form suitable bland powders which can be dusted on as a protective and cooling application to an inflamed surface, *e.g.*, in erythemas, in dry scaly dermatitis and in herpes zoster. They are only useful when the eruption is of a dry nature, because if there is any discharge the powder cakes and acts as a mechanical irritant. Drugs such as boric acid, salicylic acid and iodoform may be added to these inert powders in a proportion of 1 to 2 per cent. They are dredged on the skin and form a clean preparation which is cooling and easy to remove. At certain stages in inflammatory skin diseases the best results may be obtained from the application of powders alone.

**Watery Pastes.**—Powders may be mixed with water to form a substance having the consistence of a paste, and these watery pastes are sometimes useful in acutely inflamed erythematous eruptions, particularly in acute sunburn.

**Poultices.**—The only poultice which is really efficacious and of outstanding value in the treatment of skin diseases is the starch poultice. It is made in the following way, using either wheaten or maize starch:—

To make a starch poultice for the scalp, four tablespoonfuls of starch, one teaspoonful of boracic and one pint of water are required. Double this amount is needed for a poultice for the hand and arm. The starch is put into a basin and the boracic, after being crushed to a powder, is added to it. It is then mixed with cold water until it forms a thick cream. Boiling water is added until the diluted cream sets into a jelly. During this addition the mixture is stirred continuously with a wooden spoon. The jelly so obtained is beaten with the spoon for a few minutes until the starch is smooth, and it is then left until quite cold.

The cold jelly is spread in a layer about  $\frac{3}{4}$  in. thick on a piece of strong calico, leaving a margin all round. It is then covered with gauze and the margin folded in. The poultice should be of such a size that it extends 1 in. beyond the margin of the affected area. Where the use of a poultice spread in this way is not possible owing to anatomical difficulties such as are met with in a body fold, the starch jelly should be rolled in a single layer of gauze and bandaged on. When a whole limb is being treated with starch poultices, two should be made and applied to the upper and under surfaces so as to overlap at the sides.

The ordinary washing starches do not produce as good a jelly as do wheaten, maize, or even potato starches. If desired, the initial paste may be made with 2 per cent. aqueous solution of gentian violet or 1 : 1,000 aqueous solution of acriflavine instead of ordinary water. A charcoal starch poultice may be obtained by adding 1 to 2 drachms (3.9 to 7.8 gm.) of charcoal to the cold-water paste before the addition of boiling water.

The application of starch poultices is a universally safe treatment for all exudative forms of skin disease, and with ingenuity they can be applied and retained in position on any part of the body. Their disadvantage is their weight and sometimes the feeling of clamminess which they produce.

When starch poultices are being used it may be necessary to keep the patient in bed in order to allow applications to be made and to be kept in position. It is particularly important to avoid a hard edge of linen or calico coming into contact with the eruption. The poultices should lift off easily and leave, practically speaking, no starch adherent to the skin surface. They absorb exudate into their substance and thus reduce the chance of the dressing causing a spread of infection by the retention of discharges, or by their extension to adjacent areas as is liable to happen with ordinary occlusive wet dressings. Starch poultices are difficult to make, and if not made properly they may either be lumpy, too moist, or may dry to a cement-like consistency after an hour or two, and in consequence do considerable harm. They should be renewed every four or five hours, and as good poultices come cleanly off the skin, washing the part once daily is all that is required. In this way a minimum of interference with an inflamed surface is ensured.

**Lotions.**—Lotions may contain medicinal substances either in solution or in suspension. A lotion commonly employed is one containing glycerin and an inert powder in addition to the medicinal substances dissolved or in suspension in the fluid vehicle. Lotions are usually made up with water, but spirit may be added to the water, and some lotions are entirely spirituous. Lotions may be applied either by dabbing or painting them on with a pledget of cotton-wool or a brush, or by applying strips of calico or linen soaked with the lotion which are then covered with some occlusive material such as oiled silk or jaconet. If the surface to be treated is extensive, the lotion should be brought to blood heat before use. A powdery lotion when painted or applied to the surface has a cooling effect due to the evaporation of water, and thereafter a thin layer of powder is left on the skin surface which remains adherent on account of the glycerin contained in the lotion.

Lotions are useful because they are easy to apply, are clean and in virtue of their cooling effect are efficient in allaying itch. They are used in inflammation of the skin in all its forms, and they may be applied, even as occlusive dressings, to large areas of the body surface. Lotions are removed by gentle washing with soap and water, if necessary after a preliminary softening with olive oil. Should some of the lotion become adherent to an irritable surface it should be allowed to remain, because vigorous rubbing will only further irritate and inflame the area.

**Ointments and Pastes.**—Ointment bases may be either animal fats or mineral oils of suitable consistence, and these substances may be used alone or in the form of water in oil or oil in water emulsions. An example of the former is unguentum aqua rosæ, and the latter may be compounded by adding an emulsifying agent such as lanette wax s.x. to a mixture of the greasy base and water:

Lanette Wax	.	.	.	.	oz. 1 (31 gm.)	.
Paraff. Liq.						
Aq.	.	.	.	.	āā fl. oz. 1 (28·4 c.c.)	

\*For practical purposes, lard, hydrous wool fat and soft paraffin are all the bases which are required. The addition of wax, eucerine, spermaceti, stearines, etc., is quite unnecessary; these substances merely giving a smoother feel to the base. Ointments are used as a vehicle for the application of all types of chemicals to the skin. They may be rubbed in, or applied spread on



strips of linen or calico which are then bandaged on to the part. When rubbing is carried out the palm of the hand should be used in preference to the finger tips, the inunction being performed with steady even pressure and in a unidirectional manner if the part is hairy.

An ointment may be stiffened by the addition of an inert powder such as zinc oxide or starch to give it the consistence of a paste. The same medicinal substances may be incorporated in pastes as in ointments. Pastes cannot easily be rubbed in unless they are very thin, that is to say, containing not more than 10 to 15 per cent. of powder; if they are stiffer they must be applied spread on strips of calico or linen varying in width from  $\frac{1}{2}$  in. for the fingers to 3 in. for the limbs. If the trunk has to be dressed, material is shaped to fit, overlapping the shoulders and sides and cut to clear the axillæ. For the head and face a mask is used, and this should always cover the head, even when the face only is being treated. The material is pinned at the head and sides of the neck and kept in position with a bandage. A mask which only covers the face and is not carried over the head will invariably slip out of position and be uncomfortable. Pastes cannot conveniently be applied to surfaces covered with hair, and should their application be necessary to such areas the part must be shaved. Pastes are, generally speaking, more useful than ointments, although they are more difficult to apply. Being stiffer in consistence than ointments, they lend more support to the area to which they are applied, and a certain amount of exudate may penetrate into the interstices of the paste. Although it cannot be demonstrated that a paste is capable of absorbing water or serum, there is no doubt that pastes can be applied to exudative lesions with benefit, whereas ointments are unsuitable applications if there is much exudation from the skin.

Pastes should not be made too thick because of the difficulty in removing them. Before removal the part is saturated with olive oil; it is then wiped gently with dry cotton-wool. If a great deal of rubbing is required to remove any application from a diseased skin surface, the irritation so produced may undo any good which has been brought about by the treatment. If an oil in water emulsion is used as a base it will be unnecessary to use oil as a preliminary cleansing agent as the emulsion is easily removed by soap and water alone.

In this country from 15 to 20 per cent. of inert powder added to an ointment base will give a paste which is easily applied and easily removed. In warmer climates it may be necessary to increase the quantity of powder in pastes for general use, and in certain circumstances a larger amount of powder may be required even in colder climates.

The amount of ointment or paste required for a single dressing of different areas in an adult is approximately as follows when spreads are used: (1) face, head and neck, 2 oz.; (2) hand, fingers and whole arm, 2 oz.; (3) back or front of trunk, 2 oz.; (4) entire skin surface, 1 to  $1\frac{1}{2}$  lb.

**Paints.**—Some antiseptics, and particularly the aniline dyes, are applied to the skin in the form of paints which dry on the surface. These drugs may be dissolved in water, in spirit, or applied undiluted. Paints in common use are: (1) the aniline dyes in watery or spirituous solution, (2) ichthyol and silver nitrate, either alone or combined, in watery solution, or (3) silver nitrate dissolved in spirit of nitrous ether. Crude gasworks tar in the form of a thin varnish is applied as a paint which, after five minutes, is powdered

with talc or starch. This preparation dries in about fifteen to twenty minutes and is allowed to remain on the skin for from twenty-four to forty-eight hours. It may then be removed with olive oil. It is usually advisable to apply a paste for from twelve to twenty-four hours before repainting with the tar. Wherever possible paints should be applied in watery solution to avoid any irritant effect which might be produced by spirit.

**Permanent fixed dressings** are not of great value in dermatology except in artefact dermatitis and as a final dressing in varicose dermatitis. The preparation which is least likely to irritate an inflamed or recently inflamed skin is Unna's ichthyol zinc gelatin.

## CHOICE OF TREATMENT

The choice of drug and its strength depends entirely on the type and stage of the eruption which is under treatment. Generally speaking, substances such as ichthyol, ammoniated mercury, boric acid and tar may be used in concentrations of  $\frac{1}{2}$  to 1 per cent. in the treatment of acutely inflamed conditions. If much scaling is present, drugs which have a solvent action on scales are indicated, and of these salicylic acid in a strength of 2 to 5 per cent. and tar in a strength of 3 to 5 per cent. are the most useful applications. Stronger applications for scaly and hyperkeratotic conditions are undiluted crude tar, 20 per cent. salicylic acid and 5 to 20 per cent. chrysarobin. If there is a great deal of thickening of the skin, painting with alkaline caustics may be necessary.

The use of X-rays and radium in the treatment of skin diseases requires special apparatus and special training, so that only the indications for advising such treatment need be given here. This applies also to the local treatment of lupus vulgaris with ultra-violet light.

Diathermy, carbon dioxide snow and various other destructive methods are commonly employed in dermatology, but they will not be discussed, as they play very little part in the treatment of those skin conditions to which the term medical may be applied.

## FORMULÆ FOR COMMON LOCAL APPLICATIONS

*Baths* (see preceding text).

*Lotions.*

### Calamine—

Acid. Boric.	.	.	.	.	.	.	5
Calamin.	.	.	.	.	.	.	15
Zinc. Oxid.	.	.	.	.	.	.	15
Glycer.	.	.	.	.	.	.	10
Aq.	.	.	.	.	.	ad	200

### Sulpho-Calamine—

Sulphur. Præcip. . . . .	5
Zinc. Oxid. . . . .	10
Calamin. . . . .	10
Glycer. . . . .	5
Aq. . . . .	ad 200 or 210

## Ichthammol Calamine Cream—

Ichtham.	.	.	.	.	.	.	.	1 part
Calamin.	.	.	.	.	.	.	.	1 „
Zinc. Oxid.	.	.	.	.	.	.	.	1 „
Ol. Oliv.	.	.	.	.	.	.	.	1 „
Liq. Calc. Hydrox.	.	.	.	.	.	.	.	1 „
Adeps. Lan.	.	.	.	.	.	.	.	4 parts

## Lead and Tar—

Liq. Pic. Carbon	.	.	.	.	.	.	.	10
Liq. Plumb. Subacet. Fort.	.	.	.	.	.	.	.	10
Zinc. Oxid.	.	.	.	.	.	.	.	20
Glycer.	.	.	.	.	.	.	.	20
Aq.	.	.	.	.	.	.	ad	200

## Zinc Sulphate—

Zinc. Sulph.	.	.	.	.	.	.	.	7
Potass. Sulphur.	.	.	.	.	.	.	.	7
Aq.	.	.	.	.	.	.	ad	200

(Note on application of powdery lotions.—The bottle must be thoroughly shaken and a sufficient quantity of the lotion poured into a saucer. This is further stirred with cotton-wool, and then painted on the part with the wool.)

## Gentian violet—

Gentian violet	.	.	.	.	.	.	.	1
Aq.	.	.	.	.	.	.	ad	100

To be painted on.

## Carbol Fuchsin—

Carbol fuchsin	.	.	.	.	.	.	.	2
Aq.	.	.	.	.	.	.	ad	100

To be painted on.

*Pastes.*

Base.	Zinc. Oxid.	.	.	.	.	.	.	15
	Vaselin.	.	.	.	.	.	ad	100

or

Zinc. Oxid.	.	.	.	.	.	.	.	15
Vaselin.	.	.	.	.	.	.	.	50
Lanolin.	.	.	.	.	.	.	ad	100

*Tar Applications.*

Paste.	Pic. Carbon Præp.	.	.	.	.	.	.	1 to 10
	Zinc. Oxid.	.	.	.	.	.	.	15
	Vaselin.	.	.	.	.	.	ad	100
Paint.	Pic. Liq.	.	.	.	.	.	.	15
	Benzenc.	.	.	.	.	.	.	30
	Acetone.	.	.	.	.	.	ad	100

To be painted on.

Paint. Crude gasworks tar.

To be painted on in a thin varnish and powdered.

Ol. Cadin.	.	.	.	.	.	.	.	10
Lanolin.	.	.	.	.	.	.	.	10
Vaselin.	.	.	.	.	.	.	ad	30

Apply to scalp.

*Ichthyol and Silver Nitrate—*

Argent. Nit.	.	.	.	.	.	.	.	10
Ichtham.	.	.	.	.	.	.	.	20
Aq.	.	.	.	.	.	.	ad	200

To be painted on.

*Silver Nitrate—*

(a) Aqueous.	Argent. Nit.	.	.	.	.	.	.	1
	Aq.	.	.	.	.	.	ad	200

To be applied as a wet dressing.

(b) Spirit.	Argent. Nit.	.	.	.	.	.	.	2 to 5
	Sp. Æther. Nitros.	.	.	.	.	.	ad	100

To be painted on.

*Scalp Lotions—*

(a) Resorcin.	Resorcin.	.	.	.	.	.	.	4
	Acid. Salicyl.	.	.	.	.	.	.	4
	Ol. Ricin.	.	.	.	.	.	.	3 to 4
	Sp. Meth. Indust.	.	.	.	.	.	ad	100
(b) Lactic.	Acid. Lact.	.	.	.	.	.	.	12
	Ol. Ricin.	.	.	.	.	.	.	6
	Sp. Meth. Indust.	.	.	.	.	.	ad	100

*Scalp Ointment—*

Acid. Salicyl.	.	.	.	.	.	.	.	0.5 to 1
Vaselin.	.	.	.	.	.	.	ad	30

*Chrysarobin—*

Ointment.	Chrysarob.	.	.	.	.	.	.	5 to 10
	Vaselin.	.	.	.	.	.	ad	100
Paste.	Chrysarob.	.	.	.	.	.	.	5 to 10
	Zinc. Oxid.	.	.	.	.	.	.	15
	Vaselin.	.	.	.	.	.	ad	100

*Dreuw's Ointment—*

Chrysarob.	.	.	.	.	.	.	.	20
Acid. Salicyl.	.	.	.	.	.	.	.	10
Ol. Rusc.	.	.	.	.	.	.	.	10
Sap. Moll.	.	.	.	.	.	.	.	30
Vaselin.	.	.	.	.	.	.	ad	100

To be rubbed in (never apply spread on calico).

*Peeling Paste—*

Betanaph. . . . .	2
Sulphur. Præcip. . . . .	4
Bals. Peruv. . . . .	15
Vaselin. . . . .	ad 30

*Zinc Ichthyol Jelly.*—Place solid cubes of jelly in pan and heat till cubes liquefy. Allow to cool sufficiently and then paint on skin. Flick over lightly with cotton-wool so that wool fibres adhere to painted surface. Apply a second coat of jelly and repeat flicking with wool. To remove, peel off.

At the present time it must be emphasized that economy is essential in the use of fats and oils and their derivatives, and in starch, as external therapeutic agents. In many cases paints and wet dressings can be substituted for these substances with small loss of efficiency, and dressings containing them can be applied once daily instead of twice daily. Tragacanth or acacia may be substituted for glycerin in powder suspensions, but both are unsuitable as substitutes for bases of a fatty consistence because they dry and contract the skin surface. The addition of an emulsifying agent to a fat or oil base permits of its subsequent removal from the skin with soap and water only, and in this way the use of an oil as a cleansing agent prior to washing is obviated. Such preparations are less greasy than the purely fatty or oily bases and mix readily with cutaneous exudates. A generally useful example of such an oil in water emulsion is:

Lanette Wax. S.X.	
Paraff. Moll.	
Aq. . . . .	aa 100

**BACTERIAL INFECTIONS****IMPETIGO CONTAGIOSA**

This is a superficial inflammatory condition produced by infection with a streptococcus. It is one of the commonest skin diseases and as a rule its treatment presents no difficulty, but from time to time cases are encountered which run a prolonged course and require more than ordinary care. The lesion in impetigo is a bulla, the fluid content of which is capable of producing fresh lesions. Crusting due to the coagulation of the bulla fluid is a marked feature. The aim of treatment is to kill off the infecting streptococcus without damaging the skin in the process, to absorb the exudate, thus minimizing the risk of the development of further lesions, and to render the skin in the neighbourhood of the disease as aseptic as possible.

Starch poultices should be applied at the commencement of treatment in every case in which the lesion is at all extensive. The effect of the poultice is to soften the crusts and so permit of their easy removal; it also absorbs infectious exudate, thus lessening the possibility of the development of fresh lesions. The poultices should be renewed three times daily and should be continued until exudation has become much reduced or has ceased altogether. It is often an advantage to use a 1 per cent. aqueous solution of gentian violet in conjunction with the poultices. This solution is painted on once daily,

the application being made both to the lesions and to the surrounding skin. The part should be washed at least once daily to remove any crusts and to prevent the accumulation of medicaments on the skin.

When the exudative phase has ceased a 1 per cent. ammoniated mercury paste should be used, and it is advisable to employ a fairly stiff paste, *i.e.*, containing at least 30 per cent. of powder in the greasy base. A cream containing 500 to 1,000 units of penicillin per gramme may also be found useful. Wider experience in the use of penicillin has shown that a significant proportion of patients exhibit cutaneous idiosyncrasy to it when it is applied externally. For this reason it cannot be recommended as a routine to supersede other established methods of treatment.

The poultices will, of course, have to be bandaged in position, and for the face, which is the region most commonly affected, a mask will be necessary. It is usually advisable to apply the paste spread on strips of calico or linen or as a mask. The main risk of spread in impetigo arises from scratching and from contamination of the sheets and pillows with infected discharge. It is therefore of the utmost importance that the affected part should be covered at night, even when it may not be convenient to have bandages applied during the day. If necessary, wet dressings of white lint can be substituted for the preliminary treatment with starch poultices, and gentian violet can thereafter be used alone during the exudative phase.

In young children impetiginous lesions situated on the upper lip and on the chin may be difficult to eradicate because of persistent nasal discharge, salivation and contamination with food. It is in these areas that elastoplast is useful. The part should first be painted with 2 per cent. gentian violet, the elastoplast being applied afterwards. The area may also be dabbed with a 10 per cent. solution of silver nitrate in water two or three times daily. Children suffering from impetigo also tend to infect the nail folds, and here occlusive wet dressings with 1 per cent. boric lotion are most suitable in the early stages, and an ammoniated mercury paste in the healing stages.

The treatment of impetigo of the scalp is similar to that on non-hairy areas, but it is essential to clip or shave the hair on and around the affected areas. In severe cases the entire scalp should be shaved, and in children this might almost be advised as a routine procedure in all but the most limited eruptions. It is not easy to apply starch poultices to the scalp unless a fairly large area of hair is clipped or shaved. In the occasional cases of impetigo affecting the adult scalp, shaving can sometimes be avoided by dabbing on frequently an antiseptic astringent of 5 per cent. silver nitrate and 10 per cent. ichthyol in water in the exudative stage, the hair being clipped only in the immediate vicinity of the lesions. A 1 or 2 per cent. ammoniated mercury vaseline can be used when the lesions have been dried by the lotion. Occasionally in impetigo of the scalp there is also an infection with the *pediculus capitis*, and until the parasitic element is eradicated the impetigo will persist. The pediculosis must first be treated with paraffin soaks before commencing to deal with the impetigo. Severe impetigo of the scalp, especially when associated with pediculosis, is sometimes complicated by adenitis of the cervical glands, but incision is seldom required and the glands usually subside under hot wet dressings of 10 per cent. ichthyol in water.

In the average case of impetigo no general treatment is required, and vaccines are never necessary. A proportion of children, however, tend to have frequent recurrences affecting the face, scalp, hands, knees and feet, and when this occurs the general condition of the child must be taken into consideration and measures adopted to improve the nutrition and general health. In the poorer classes one need not hesitate to hospitalize such children over a period of weeks. It should be remembered that the home surroundings may be the main factor in the causation of such recurrences, and the help of the public health authorities may have to be sought to improve them. In such recurring cases an underlying scabies must not be overlooked.

### FURUNCULOSIS

By furunculosis is meant a recurring deep staphylococcal infection of the hair follicles and sebaceous glands. The inflammatory reaction produced by such infections may eventually extend to involve the whole of the true skin, and adjacent lesions may coalesce, resulting in a greater or less degree of tissue destruction. Scar formation is an invariable result.

This brief pathological summary has been given in order to define the condition from a similar, more superficial staphylococcal infection affecting the same areas, which is more appropriately termed folliculitis, and is dealt with under the heading "Sycosis."

The treatment of individual furuncles is a simple matter. The overlying skin can be painted with 2 per cent. aqueous solution of gentian violet once daily, and hot wet dressings of 10 per cent. ichthylol in water can be applied every two to three hours. This is continued until the furuncle bursts or has been opened surgically, the core of dead tissue has been extruded or removed and the discharge has subsided. A course of penicillin injections is desirable in severe cases. Commencing furuncles are often successfully aborted by the application of elastoplast in the following way: A ring of the plaster is cut and fitted round the small swelling and then a circle of the plaster is applied to cover the entire surface. Such a dressing protects the lesion to a great extent from friction and pressure and affords it some support.

X-ray treatment is often successful in causing the rapid disappearance of a furuncle, and may be given with benefit any time up to the period when the lesion is obviously subsiding.

Difficulty arises when the lesions recur. If recurrence takes place more or less on the same part of the body, the treatment is easier than when the lesions keep on appearing at widely separated sites. In the former case, keeping the infected area continuously painted with a mild antiseptic such as gentian violet will reduce surface contamination and lessen the risk of re-inoculation with organisms. Avoidance of friction to the area is most important. • If the part is covered with hair, it should be kept shaved, and this applies to the scalp as well as to the covered areas. The commonest sites for recurring furuncles are the back of the neck, the forearms, the buttocks and the axillæ. In the axillæ the lesion is quite commonly situated in the sweat glands and not in the pilo-sebaceous system.

When the furuncles continue to appear irregularly on widely separated sites, local antiseptic prophylaxis is of less value than general measures

calculated to increase the skin resistance to the organism. Daily, or twice daily, immersion in a potassium permanganate bath is useful, and avoidance of friction is most important. Vaccines are helpful in a number of cases, and a mixed stock staphylococcal vaccine, containing a number of different strains, is usually as efficient as an autogenous or toxoid one. Injections of manganese are widely used, but their value is doubtful and the injections are painful. A liberal supply of vitamins must be included in the diet, and it is advisable for the patient to rest as much as possible.

In spite of these active and prophylactic measures, the disease may drag on for a period of months, and if this occurs it is justifiable to give a period of complete rest in bed if the patient's circumstances allow him to do so.

Every patient suffering from furunculosis should undergo a general medical examination to determine whether the condition may not be dependent on some chronic constitutional disorder, particularly diabetes. Widespread furunculosis may occasionally be due to an underlying scabies, and furunculosis in epidemic form occurs almost invariably as a complication of scabies or pediculosis.

### SYCOSIS

Sycosis is a staphylococcal infection of the orifices of the hair follicles, and occurs exclusively on areas where the hair is well developed, *i.e.*, the condition does not affect areas covered with lanugo hair. The characteristic feature of sycosis is the repetition of multiple superficial pustules on a localized area, and this is a constantly recurring phenomenon which persists for months and sometimes for years. As a result of the prolonged inflammation and contamination of the skin surface, an infective dermatitis becomes early associated with the pustular eruption, and in its fully developed state sycosis is a combination of infective dermatitis and folliculitis. The term sycosis is usually reserved for this type of eruption when it affects the beard region, but an exactly similar condition can affect the scalp, eyebrows and any other region covered with strong hair, and treatment is the same for all areas. The follicular lesions develop much less readily if the affected area is kept shaved, and they cease to develop if epilation of the area is performed. Unfortunately when the hair commences to regrow after epilation the infection may reassert itself and the follicular lesions recommence.

Treatment consists in keeping the area shaved or in producing complete temporary epilation and thereafter applying mild antiseptics. Unfortunately an area of skin affected with this type of eruption is often in a hyper-sensitive condition, so that it does not tolerate chemical applications in the same concentration as the normal skin, and in addition, to this, grease is not the most suitable application because it tends to favour pustulation.

During the first few days of treatment the removal of hair may have to be limited to clipping, as it may not be possible to shave the acutely inflamed skin, but shaving should be performed at the earliest opportunity and the area should be kept shaved. As grease is not well tolerated by the majority of cases, the local treatment is limited to painting with one or other of the aniline dyes, and the application of starch poultices; in fact, it is that



already outlined for the early stages of impetigo (see p. 166). When the inflammation has begun to subside with treatment, and this may take weeks to achieve, crude gasworks tar is a very useful application. It is to be noted that tar frequently produces pustulation, and it might be thought that it would be definitely contraindicated in sycosis. Certainly if it is applied in the form of an ointment or paste, pustulation is almost always aggravated, but its application in the crude form as a paint is much less frequently attended by pustulation, and in most cases is beneficial. Probably the reason why the inflamed skin can tolerate crude tar is that the tendency to follicular infection has subsided and the actual lesion which benefits from the tar is the complicating eczema.

Although grease is as a rule an unsatisfactory application, there is one ointment which is found to be beneficial in early cases, and it is also useful in dealing with commencing recurrences. This is a proprietary preparation, Ung. Quinolol Co. (Squibb), containing chlorhydroxyquiniline and benzoyl peroxide. It is probable that it is the chlorhydroxyquiniline which is effective, as ointments containing benzoyl peroxide alone are not efficient.

Epilation with X-rays is necessary in a large percentage of cases affecting the beard region, and a full epilating dose is given. There is often an increase in the severity of the symptoms during the first week after X-ray treatment, but by the third week, when the hairs are falling out, there is a very marked diminution in the inflammation and usually a return of the skin surface to a slightly pink but otherwise normal appearance. It will remain in this condition for a few weeks, but when the hair commences to grow again a small area of pustulation may recur and spread to involve the whole of the area originally affected. Such small areas can be again X-rayed, care being taken to screen the surrounding skin up to the edge of the area of recurrence. If the area of sycosis is a very limited one, epilation may be carried out with forceps.

Penicillin has a beneficial effect when applied locally in sycosis, either in the form of a liquid spray, or in a water soluble ointment base in a strength of 500-1,000 units per gramme. Its parenteral administration has no effect on the disease. In some cases which have resisted X-ray therapy and antiseptic dressings properly applied over a prolonged period, penicillin has brought about a marked and sudden amelioration of the eruption. It has been found that penicillin must in general be used for a number of weeks, even although the initial improvement is rapid and the gross staphylococcal infection of the skin quickly reduced in amount. It must be remembered that some degree of eczema is present in all longstanding cases of sycosis and this component of the eruption is not influenced by the drug. Relapse is prone to occur after an apparent cure. At the present time it may be said that penicillin, while not a specific for sycosis, is a valuable addition to the existing methods of treatment for this stubborn disease. The possibility of the existence of cutaneous idiosyncrasy to its external application must be kept in mind.

Vaccine therapy has not proved useful in this condition, probably owing to the fact that the lesions are superficially situated as compared with furunculosis. Staphylococcal antiviral applications do not seem to have any specific effect on the disease, but in some cases they act as soothing dressings in the same way as starch poultices.

## PARASITIC INFECTIONS

### RINGWORM

Infection of the skin with the various types of ringworm fungus produces a number of eruptions which are more or less characteristic for the type of infecting fungus and for the site affected. The treatment of such conditions is simply directed towards the destruction of the parasite, and the difficulties encountered are due to its situation in the skin, its normal resistance to antiseptics and the susceptibility of the skin—and particularly the inflamed skin—to chemical irritation.

**Ringworm of the Body.**—When a fungus infects the non-hairy non-flexural surfaces its destruction is a fairly easy matter. With the exception of the palms and soles where the stratum corneum is thick, the fungus is situated on and very close to the surface, is easily accessible to antiseptics and the area can readily be cleansed. In *tinca corporis*, therefore, repeated painting at daily intervals or every second day with a 2½ per cent. tincture of iodine or basic fuchsin paint is usually all that is required to eradicate the condition in from ten days to a fortnight. Unguentum iodidi rubbed in twice daily is equally efficient. In infections with virulent fungus derived from an animal source, it may be necessary to commence treatment with starch poultices and gentian violet to allay the acute and often purulent inflammation, and to use iodine in the later stages. As an alternative to the iodine treatment an ointment containing 6 per cent. benzoic acid and 3 per cent. salicylic acid may be prescribed, to be rubbed in twice daily.

**Ringworm of the Scalp.**—This presents a much more difficult problem because the fungus is present inside and surrounding the hair shaft in its intrafollicular portion, and in this situation it is exceedingly difficult for antiseptics to reach it. It is therefore necessary to epilate the scalp either by means of X-rays or thallium in order to get rid of the infected hairs, and so to permit the entrance of antiseptics into the follicles. The technique of X-ray treatment of the scalp is difficult, and as it requires considerable knowledge of superficial X-ray therapy it need not be dealt with here.

Epilation with thallium acetate is an easy procedure in children, but one which must be carried out with scrupulous attention to detail, because thallium is a dangerous drug producing severe constitutional symptoms and possibly death if wrongly used. Thallium has gained an unfortunate reputation in some parts of this country because of one dispensing error which had a fatal result. A similar error in the dispensing of arsenic or strychnine might have led to equally disastrous results without these drugs falling into disrepute, and the toxic properties of thallium need not, therefore, contraindicate its use. The criticisms which have been levelled against thallium are applicable to all poisonous substances employed in medicine.

The dose of thallium is calculated for each individual case, the child being given 8.5 mg. of thallium acetate for each kilogram of naked body-weight. The calculated amount is given in a single dose and is not repeated. Following its administration a mild constitutional upset is noticed three or four days afterwards in about 30 per cent. of children. This takes the form of temporary lassitude associated with rheumatic pains in the legs. The symptoms last only for a few days. From seventeen to twenty-one

days after the administration of the epilating dose the hair commences to loosen and can be plucked out painlessly all over the scalp; the eyebrows are not affected. Compared with X-ray epilation the fall of hair due to thallium occurs earlier and is less complete, and the regrowth of hair takes place more rapidly. With thallium it is therefore essential to supervise the epilation of the scalp to make certain that it is thorough, and to carry out antiseptic measures in a most careful and vigorous fashion. Thallium should not be administered to a child weighing over 30 kg. unless in very special circumstances, when a dose may be given to children weighing up to 36 kg. It is a drug which must never be given to adolescents or adults for purposes of epilation because of the severe toxic symptoms which result.

Following a dose of thallium, epilation will occur and regrowth of the hair to a length of about half an inch will take place during a period of approximately three months. In addition to epilating measures, antiseptic treatment must be applied to the scalp twice daily and the scalp must be washed once daily during the entire period of depilation and regrowth.

The treatment of ringworm of the scalp would therefore be as follows:—

After a diagnosis has been made, the hair is clipped short all over the scalp, and this may reveal the presence of hitherto unsuspected patches of disease. The scalp is then treated twice daily with a 10 per cent. sulphur ointment, and it is an advantage to paint on 2 to 5 per cent. tincture of iodine twice weekly in place of the ointment. Epilating measures are carried out as soon as possible. The antiseptic treatment is continued during the period of epilation and regrowth until the new hair has reached a length of about half an inch. Treatment and washing are then both stopped altogether for a period of three weeks, at the end of which time the scalp is examined. If any fungus has escaped destruction by the antiseptic the disease will become apparent during the three weeks in which treatment has been discontinued. During the entire course of treatment the child should wear a paper lining inside the cap, and this should be renewed daily, the old lining being burnt. All contacts should be carefully examined for the presence of disease, and, of course, an infected child must not attend school.

The infiltrated lesions known as kerion, which are produced by infection with virulent fungi derived from animals, do not require epilation because they cure themselves in from three to four months' time by the production of a natural immunity to the fungus. All that is necessary in treatment is the relief of pain by starch poultices or wet dressings in the early stages, and the limitation of secondary infection by means of a 1 per cent. ammoniated mercury paste when the phase of infiltration is subsiding. Similar measures are used for ringworm of the beard, a condition which must be differentiated from sycosis, and one which, like kerion, runs a self-limiting course calling only for palliative treatment.

**Ringworm of the Body Folds** (Epidermophytosis).—Infection with the epidermophyton fungus occurs in the areas between the toes, in the groins and less frequently in other body folds. The infection may extend from the interdigital areas to involve the soles of the feet, and the palms of the hands may also become affected. A great variety of antiseptics have been used in the treatment of this particular type of fungus infection, but while many

are efficient it cannot be said that any one of them is outstanding. Tincture of iodine in strengths from 0.5 to 5 per cent. may be used according to the tolerance of the individual skin, and swabbing the area with a 3 to 5 per cent. solution of silver nitrate in spirits of nitrous ether is a clean and useful method. If there is marked secondary infection with pyogenic organisms, a 2 per cent. solution of gentian violet may be used in the early stages. When the condition has reached a dry scaly stage, an ointment containing 6 per cent. benzoic acid and 3 per cent. salicylic acid should be used in preference to lotions. X-ray treatment is useful in cases which do not respond to these measures.

Should the fungus produce an intense inflammation of the skin, the more vigorous remedies may have to be withheld for the time being. Soothing applications such as starch poultices or wet dressings of boric acid solution or a solution of 10 per cent. ichthyol in water should be used until the acute inflammation—which is often associated with secondary pyogenic infection—has subsided. In the acute vesicular pompholyx-like eruptions which affect the soles, palms and the sides of the fingers, wet dressings of  $\frac{1}{2}$  per cent. silver nitrate in water are most beneficial. They are applied twice daily for three or four days, and usually cause rapid desiccation of the vesicles and prevent the appearance of fresh ones. At the end of that time a 1 per cent. ichthyol paste is used and finally the benzoic and salicylic vaseline should be applied.

Infections of the feet are extremely stubborn and resistant to treatment, and it is doubtful whether the infection can ever be completely eradicated from this area. When the condition seems to be in abeyance the individual should be advised to apply an antiseptic, such as tincture of iodine, periodically to the affected areas.

Ringworm of the groin is much more amenable to treatment than ringworm of the feet, and if thoroughly treated its disappearance can be assured.

In all cases of epidermophyton infection, care must be taken to disinfect wearing apparel, and especially all the articles with which the infected person comes into contact in the bathroom, *i.e.*, bath mat, floor, etc. In a private house there is no need to anticipate a spread of the infection provided reasonable precautions are taken. The disease is usually acquired from the floor of dressing-rooms, swimming baths, Turkish baths, *plages* and, in infection of the groin, from lavatory seats. When an object or room has once become infected it is often a difficult matter to secure complete destruction of the parasite even by the use of strong disinfecting measures. The condition is so prevalent that no attempt at isolation can be made, as the number of very slight unrecognized cases far outweighs the number which exhibit active signs of disease.

**Ringworm of the Nails.**—Infection of the toe nails and finger nails may occur as an isolated event, or the nails may become infected from already existing lesions on other parts of the body. The difficulties in treatment are comparable to those met with in ringworm of the scalp, and as in the case of the hair, removal of the nail is essential to rapid cure. Surgical removal is probably best, although it may be difficult in some instances on account of the friability of the nail plate. After surgical removal strong antiseptic paints, such as 5 per cent. tincture of iodine, are applied to the nail bed and nail fold as soon as possible, and are continued during the whole period of regrowth of the nail. The patient must be informed about

the difficulty of destroying the fungus and the risk of reinfection of the new nail plate. He should be advised to take this risk, however, because if the nail is not removed there is no chance of the disease being cured or disappearing spontaneously. Infection of other parts of the body from an infected nail, although a possibility, is uncommon, and experience shows that an individual suffering from ringworm of the nails need not be considered a grave source of danger to others.

### SCABIES

Scabies is a disease which, if neglected, can produce considerable incapacity in large masses of people. The accompanying irritation alone is often a serious feature on account of loss of sleep and consequent loss of efficiency, and the impetigo and furunculosis which may complicate the disease can cause incapacity of a major type. The economic effect of this is self-evident, and under war conditions the results of the disease may be serious from a military point of view.

At the present time 5 per cent. sulphur ointment or 25 per cent. emulsion of benzyl benzoate are the two most satisfactory and certain methods of treatment. The former is the cheaper, but takes longer; it is the more suitable of the two for severe cases. The latter is expensive but rapid and clean, and is sufficiently certain in cases of medium severity.

Sulphur treatment is carried out as follows: The patient steeps in a bath for twenty minutes, lathers all over with soft soap and scrubs the affected areas with a soft nailbrush to open up as far as possible the burrows of the *acarus*. Thereafter a 5 per cent. sulphur ointment is rubbed in thoroughly all over the body with the exception of the head. The inunction is repeated at intervals of twelve hours, till six applications have been made. If convenient the legs, feet, arms and hands may then be bandaged, thereby enhancing the lethal effect on the parasite. Twelve hours after the last treatment a bath is given, clean underwear worn and the bedding disinfected. In mild cases four, or in urgent circumstances two, inunctions only may be given.

If there is a severe complicating impetigo it should be treated in the usual way for a few days before sulphur ointment treatment is begun.

The patient is usually free from itch after the first or second inunction, and he remains so unless the sulphur irritates his skin. A few patients develop a mild dermatitis after the six applications, but this yields readily to a calamine or lead and zinc lotion used for a few days after cessation of the sulphur treatment. Recurrence of the irritation in a week to ten days after treatment has been completed means a recurrence of the disease, either due to inefficient treatment or to reinfection.

Speed has been mentioned as an important factor when large numbers of individuals have to be dealt with, but it must be borne in mind that the severity of the disorder determines the rapidity of cure to a greater degree than the choice of parasiticide. Considering only the destruction of the *acarus*, and taking no account of the cure of septic complications, the duration of the contact of the parasiticide with the skin surface is a definite factor in the cure, and the time required will naturally vary with the extent and severity of the infection. In conjunction with the time factor the more intimate the contact of the parasiticide with the skin, the greater

will be its efficiency, and in this respect the rubbing in of sulphur in a greasy base is the most satisfactory method. Grease has the slight disadvantage of soiling underwear, but boiling the clothes overcomes this drawback. The subsequent steam sterilization of the fomites, which must be carried out no matter what method of treatment is used, is a more destructive process than the therapeutic application of grease.

The efficiency of sulphur has been adversely criticized because of the occasional development of sulphur dermatitis. This complication is, however, due less to the efficient intensive use of a 5 per cent. sulphur ointment over a period of three days than to the inadequate intermittent use of such an ointment over a prolonged period, or to the use of undiluted 10 per cent. B.P. ung. sulphur.

Benzyl benzoate treatment is carried out as follows: A mixture composed of equal parts of benzyl benzoate (25 per cent.) and lanette wax (2 per cent.) in water is painted all over the body with a brush. The solution is allowed to dry on the skin surface and a second coating is applied. The following day a bath is given. If it is thought necessary the application of benzyl benzoate emulsion may be repeated daily or twice daily for two or three days, and while clean underwear is worn twelve hours after the last treatment, the bath may be postponed for a further period of two days.

Recently tetraethylthiuram monosulphide (tetmos) has been used successfully in the treatment of human scabies. The following formula is employed: tetmos 25 per cent.; polyglycerol ricinoleate 10 per cent.; industrial spirit 65 per cent. This emulsion is diluted in the proportion of one part to four parts of water, giving a strength of 5 per cent. tetmos. The diluted emulsion is smeared over the body morning and night for two or three days. Tetmos has also proved curative when incorporated in a soap in a strength of five per cent., and the routine use of such a soap in communities infested with scabies has been shown to bring about a marked reduction in the incidence of the infestation.

Moderately severe, severe, and infected patients should have the treatment with 5 per cent. ung. sulphur. Confinement to bed is essential in all infected cases, for although the parasitic element is eliminated in three days, the entire treatment of a severely infected case may cover a period of four to six weeks.

It is important to examine and, if necessary, to treat all contacts and also to make sure that the infected bedding has been adequately disinfected, although it must be admitted that fomites do not play an important part in the transmission of the disease. The search for infected contacts and the proper handling of fomites may throw considerable strain on the public health services.

### PEDICULOSIS

**Pediculosis capitis.**—The prevalence of *Pediculosis capitis* is greater than is generally realized. It may be treated by means of common paraffin oil in the following way: The forehead, ears and neck are first protected with zinc ointment, then, with no preliminary washing, the hair and scalp are soaked with paraffin. Strips of calico soaked in paraffin are applied to the scalp and covered over with an improvised cap of jaconet or with a rubber bathing cap. The soaks are repeated after twelve hours, and according

to the result they may be reapplied at twelve-hourly intervals for a further twenty-four hours. After the last application has been removed the scalp is washed. The adult parasites are readily killed by this method, and the nits can later be removed by combing with a small tooth comb which has been dipped in weak acetic acid. Oil of sassafras, xylol, and 1 in 40 aqueous solution of carbolic acid may be used in the same way as paraffin oil.

Recently it has been found that a mixture containing 25 per cent. lauryl thiocyanate in refined liquid paraffin ("Lethane Oil") is capable of destroying the parasites, and it is a more pleasant method of treatment than those hitherto in use. The mixture is rubbed into the scalp once only, and the scalp is left unwashed for ten days, during which time the lauryl thiocyanate exerts its action on the pediculi and nits.

If the infection is severe, the nits numerous, and an extensive impetigo present, it may be necessary as a preliminary measure to cut, and subsequently shave, the scalp (see Impetigo). No matter how impetiginous the scalp may be or how severe the accompanying adenitis of the cervical glands, the pediculosis should be dealt with in the first instance. The associated impetigo and adenitis are treated in the ordinary way, but it is seldom necessary to incise the glands.

Dichlor-diphenyl-trichlorethane (D.D.T.) (see p. 277) is a recently introduced parasiticide which is lethal to all varieties of pediculus and many other parasites which infest man, animals and plants. It can be applied as an emulsion, which in a strength of 2 per cent. has proved a most effective remedy. Its action is exerted on the adult parasites and larvæ but its ovicidal action is weak. Its efficiency is due to the fact that, like lethane oil, it persists on the skin and hair and so kills the larvæ as they hatch out. D.D.T. can also be used as a powder with which to impregnate garments.

**Pediculosis pubis.**—This is treated by lethane oil or D.D.T. emulsion, and in some cases it may be advisable to shave the hair at the commencement of treatment. It should be remembered that the hair of the natal fold, trunk, axillæ and eyebrows and lids can be infected with this parasite.

**Pediculosis corporis.**—This is treated in the same manner as scabies, and a bath followed by one or two inunctions of sulphur ointment, and disinfection of the underwear, is usually sufficient to eradicate the infection. To prevent re-infestation the undergarments can be dusted with 5 per cent. D.D.T. powder in talc.

Pediculosis pubis and corporis are apt to occur in sudden widespread epidemics when conditions lead to overcrowding. Compared with scabies the spread of this type of parasitism is more rapid, but when bathing and laundry facilities become available its control is a simple matter. These differences are due to the greater inherent mobility of the louse as compared with the acarus, and to the fact that it dwells on the clothing and on the skin surface and not in the skin substance as does the acarus. In crowded communities parasiticism is the most common predisposing factor in the development of boils.

## ACNE

While there is little doubt that the development of acne is ultimately dependent on the functions of the endocrine glands, the main treatment of the condition is essentially local. Overactivity of the sebaceous glands seems to be the important local predisposing factor in the development of

the condition. It results in the formation of the comedones, fosters the growth of pyogenic organisms and so predisposes to pustule formation.

The local treatment of acne consists of (1) methods to keep the skin surface as free from oil as possible, (2) the external application of drugs which seem to have an inhibitory effect on oil formation, (3) the administration of X-rays and (4) internal treatment for the reduction of the functional activity of the sebaceous glands. Frequent swabbing of the affected area with ether or surgical spirit may be advised to remove the surface grease. Once daily, preferably at night, the face is very thoroughly washed with hot water and sulphur soap and the lather massaged into the skin for a few minutes. The lather is then removed, the face dried gently, and thereafter the following lotion dabbed on:—

R7	Zinc. Sulph.	.	.	.	.	dr. 1 (3.9 gm.)
	Potass. Sulphur.	.	.	.	.	dr. 1 (3.9 gm.)
	Aq.	.	.	.	ad	oz. 4 (114 c.c.)

The lotion leaves a powder on the skin and this is allowed to remain on overnight and is washed off in the morning. After a week or ten days of this treatment the following peeling paste may be used:—

R7	Betanaph.	.	.	.	.	2 gm.
	Sulph. Præcip.	.	.	.	.	4 „
	Bals. Peruv.	.	.	.	.	15 „
	Vaselin.	.	.	.	ad	30 „

The paste is smeared on the affected areas at night and removed in the morning with olive oil. Immediately after its application it causes a good deal of nipping and burning, which lasts for about a quarter of an hour and then subsides. The effect of the paste is that of an antiseptic and counter-irritant, and it causes the skin to become slightly inflamed and subsequently to peel. This desquamating effect clears the mouths of the follicles, thus facilitating the removal of blackheads and dammed-up sebaceous material, and, in virtue of the antiseptic action of the paste, surface infection is reduced. It is not as a rule possible to apply the peeling paste for more than two consecutive nights because of the amount of inflammation it produces, and to allay this an ichthyol paste is used every third night. After about three weeks' preliminary treatment on these lines X-ray treatment may be commenced, and while this is being given it is better to stop all active local treatment and merely to use mild applications such as calamine lotion. It may be said that X-ray therapy is essential at some stage in the treatment of all but the mildest cases of acne. X-rays are best administered in fractional doses once weekly, and a course consists of four to six doses spread over a period of six weeks, the total amount of X-rays given during that period being not more than one and a half skin doses. The X-rays have an inhibitory action on the sebaceous glands, thus reducing the amount of oil secretion, and producing a beneficial action on the whole of the exposed surface.

Internal measures are limited to the administration of iron, the regulation of the digestion and the reduction of carbohydrate intake, especially the actual sugar content of the diet.

Vaccine therapy is only useful in cases in which deep-seated pustulation



is a feature and is of no value when comedones, superficial pustules and seborrhœa are the main features.

Recently 1 mg. of stilbœstrol dipropionate daily has been used with some success, especially in those cases occurring in girls when there is a history of exacerbation of the eruption just before or during a period. Even with this small dose some degree of nausea may sometimes occur.

It is important to see cases of acne at frequent intervals whether or not X-ray treatment is being given, because, to achieve rapid improvement, all large blackheads should be removed from the affected area and pustules incised with a narrow-bladed knife.

It is also necessary to see that the scalp is washed regularly, because it is invariably greasy and often scaly. Organismal contamination in these circumstances is abundant, and the chance of pustulation due to infection from the scalp is increased.

## ROSACEA

Rosacea is almost always associated with one or more of the following conditions: A certain amount of seborrhœa of the face; seborrhœa and pityriasis of the scalp; a mild degree of indigestion; symptoms indicating slight ovarian dysfunction. The local predisposing factors are a marked tendency to capillary flushing, very open pores and an increased virulence in the organisms which normally contaminate the surface. Treatment may therefore have to be directed towards the correction of one or all of these contributing causes. A sulpho-calamine lotion is probably the best local application, and it may be helpful to alternate it day about with either a 1 per cent. sulphur paste or a 1 per cent. ichthyol paste. In addition to daily treatment, weekly fractional doses of X-rays given in the same way as for acne are almost essential for rapid cure. If possible the individual should avoid undue exposure to sunlight, heat and cold winds. The scalp must be kept clean by frequent washing, and, if necessary, the application of a 2 per cent. salicylic vaseline or a lotion containing 1 drachm (3.6 c.c.) each of salicylic acid, resorcin and castor oil in 6 oz. of spirit.

The diet should be plain, all spicy foods should be eliminated from it, and the patient should be instructed to allow all hot fluids to become cool before they are ingested. Some patients will be found to improve if alkali is given after their main meals, and in others the administration of dilute hydrochloric acid is helpful. Neither the eruption nor the history may give any indication as to which of these remedies will be efficacious, and it is hardly worth while to carry out a test meal to ascertain the exact state of the gastric secretion.

Vaccine therapy is of little value in rosacea even when pustulation is marked.

If rosacea is treated in its early stages the affected skin will return to normal and the vascular dilatation will subside. If, however, the eruption has been present for some time a permanent capillary dilatation is almost inevitable, and the only way to diminish the redness at that stage is to obliterate as many of the dilated vessels as possible by diathermy coagulation. The results of diathermy coagulation in suitable cases are often most satisfactory to the patient if the treatment is persevered with over a period of months.

## ECZEMA

Eczema is a specific type of skin reaction characterized by superficial inflammatory oedema of the epidermis associated with vesicle formation. After a longer or shorter time this reaction passes through a scaly phase towards healing. It is an exceedingly common type of eruption and one which requires the utmost care in its treatment. A skin which is affected by eczema is one which has shown an idiosyncrasy to some irritant. This being so, a further idiosyncrasy to one or more of the drugs which are commonly used in the treatment of the disease is encountered in a number of cases. The irritant factor which has caused the eruption may continue to act for a considerable time after treatment has been instituted, and for this reason the fact that treatment has been commenced does not ensure that the eruption will from that time forward proceed towards healing. Sometimes the patient carries out the treatment prescribed in a most inefficient way, or else he exposes the eruption to irritation with dust or liquids or mechanical trauma while under treatment, and these injuries, however slight, will counteract any beneficial effects which may have been obtained. There is no reason why a large proportion of patients should not be fairly easily and quickly cured if treatment is commenced soon after the appearance of the rash, and provided a correct diagnosis of the type of eczema has been made. Recrudescence and recurrence are common features of eczema. In a number of instances they might be avoided if an existing eruption were treated till complete cure was obtained, and if adequate precautions were taken to protect the area of skin which had recently been affected from obvious sources of irritation. It is only too common to observe a patient who applies treatment enthusiastically until the rash has almost disappeared, and then, satisfied with the partial result obtained, he discontinues treatment, neglects the care of his skin, and wonders why the eruption flares up again. It is important to ensure a period of rest and protection for an area of skin which has been the seat of eczema for some weeks or even months after it has been cured.

Eczema can be divided into two main groups, first, those in which an irritant affects an idiosyncratic skin from the outside, and secondly, those in which the irritant reaches the idiosyncratic skin via the blood stream. Fortunately the external cases predominate numerically, for when the irritant is derived from within, treatment is much more difficult and the tendency to recurrence greater.

### ECZEMA DUE TO EXTERNAL CAUSES

**Eczema due to Light.**—This is a most distressing condition, for obviously it is difficult for an individual to avoid entirely exposure to sunlight. The local treatment consists in the application of a 1 per cent. ichthyol paste at night as a healing measure, and during the day an ointment containing 1 to 2 per cent. quinine sulphate may be used as a protection against the sun's rays. Another application which sometimes affords protection in mild cases is a 2 or 3 per cent. solution of tannic acid in equal parts of spirit and water. Apart from treating the skin, all reasonable precautions must be taken to avoid direct exposure to sunlight.

*Internal Treatment.*—A proportion of mild cases are greatly relieved by a course of peptone injections in early or middle spring, a procedure which seems to increase the skin resistance to light irritation and one which should always be tried. A 10 per cent. solution is used and the injection given twice weekly subcutaneously over a period of three weeks, the initial dose being 0.5 c.c., and this is gradually increased to 2 c.c. A small number of patients benefit if wheat is excluded from the diet, and in them it would appear that some chemical complex in the wheat sensitizes the epidermal cells to sunlight. Other dietary modifications do not seem to have any influence on the condition.

*Eczema due to External Chemical Irritation.*—If the external application of a chemical to the skin has produced eczema, the eruption, left to itself, may take as long as two months to subside, even when all further contact with the irritant has ceased. Under treatment the rash should disappear in a much shorter period. If, however, it has been present for some considerable time prior to the commencement of treatment, the skin may have undergone anatomical and probably functional changes due to the prolonged inflammation, and these changes retard the healing process. The object of treatment is to provide a protective soothing covering to the affected area. If the eruption is in an acute vesicular exudative phase stage, starch poultices are indicated. Whenever the exudative has subsided the application of a 1 per cent. ichthyol paste spread on linen or calico is all that is required. If secondary infection is present the methods used in the treatment of infective eczema will have to be instituted (see below). If hypertrophy of the skin has taken place as a result of a long-continued inflammation, it will be necessary to use crude gasworks tar, and perhaps X-rays as well, to aid the dissipation of the chronic dermal infiltration.

Every effort should be made to determine accurately the chemical cause of the eruption, and for this purpose a careful history is necessary, followed by patch tests with all the irritants suspected of being of ætiological importance. Specific desensitization to a discovered irritant, while it has been successfully carried out in isolated cases, is not as yet a procedure which is generally serviceable.

*Infective Eczema.*—As the cause of this condition is almost always a streptococcus, staphylococcus or yeast, the treatment is essentially antiseptic and is in many ways similar to that employed in impetigo and sycosis. The type of rash varies according to its situation, but on any area it may present an exudative stage followed by a dry scaly stage. In the exudative phase gentian violet and starch poultices may be used, or wet dressings of  $\frac{1}{2}$  per cent. silver nitrate in water. Crude tar may be tried as soon as the exudative phase has subsided. An ichthyol paste can be used for a day or two between the discontinuation of the starch, gentian violet, or wet dressings, and the commencement of the crude tar. It is remarkable how an acutely inflamed but only slightly exudative patch of infective eczema will tolerate crude tar treatment and improve under it. It is important in infective eczema situated in the flexures to continue treatment until every vestige of inflammation in the deepest part of the fold has disappeared. X-ray treatment is useful for patches of infective eczema affecting the backs of the hands and the dorsum of the feet, but it is not very helpful in flexural infective eczema. It is to be noted that flexural fungus infections will stand much stronger concentrations of anti-

septics than eczema of the flexures due to bacterial infection (see Ringworm). Infective eczema, like sycosis, may be intolerant to grease for considerable periods during the course of treatment.

### ECZEMA DUE TO INTERNAL CAUSES

It is rare to discover the exact cause of an eczema which, from its distribution, course and history, is obviously of internal origin. Occasionally one single article of diet is found to be responsible, but usually no causal relationship can be established between the diet and the rash. The removal of areas of focal sepsis may be followed by the rapid disappearance of the rash, but this is only occasionally noted. While the diet should be investigated and attention paid to areas of focal sepsis in every case, active general treatment may resolve itself into carrying out procedures to ensure free elimination, *i.e.*, the administration of fluids in quantity and saline purgatives. Local treatment consists in the application of tar preparations in the form of lotions or pastes, and later as crude tar, and the avoidance of friction which tends to localize the eruption and possibly to precipitate fresh patches. Grease sensitivity is much less marked in eczema arising from internal causes. When it is noted in the more acute phases of the eruption which would otherwise be treated with pastes, the use of a lead and tar lotion or  $\frac{1}{2}$  per cent. silver nitrate soaks may be necessary until it is in a condition deemed suitable for crude tar. Localized patches of internal eczema sometimes respond in a most satisfactory way to X-ray therapy, and this is especially so in the chronic lichenified patches of eczema seen in elderly people usually situated on the nape of the neck, the sacral region, the thighs or the outer aspects of the forearms.

**Infantile Eczema.**—Although a great deal of work has been done to ascertain the rôle of diet in the production of this type of eruption, it is only in exceptional instances that a specific protein can be legitimately incriminated as the cause. Nevertheless the condition seems to be undoubtedly associated in some vague manner with the gastro-intestinal tract, and while gastro-intestinal symptoms are by no means a frequent accompaniment, alteration or modification of the diet seems to be necessary in many cases as an adjuvant to local treatment. In practice it is advisable to change the diet completely in every case, and to ensure that the feeds are given properly and at regular intervals. As a substitute for fresh milk a dried milk preparation, either human or bovine, is probably the best type to use. If goat's milk is available it should be tried, and increasing the fat content of cow's milk by adding 1 oz. of suet in a muslin bag to 1 pint of milk and boiling for twenty minutes makes a mixture which is often well tolerated. The addition of a little citrate of magnesia to the milk may also help. Orange juice aggravates the eruption in a number of cases, and it is perhaps wise to omit it from the diet and substitute grapefruit juice, tomato juice or spinach strainings. The daily supply of vitamins A and D should be ensured by suitable additions. Syrup of figs should be given twice weekly, and in older babies the bowel may be washed out.

The local treatment consists in the application of tar preparations, the protection of the affected skin with bandages and the immobilization of the arms and legs with splints. Such restraint is a most important feature because a scratch habit is almost always present in infantile eczema, and

scratching with the hands and feet and rubbing on the bedding greatly aggravates the eruption. In the vesicular stage a lead and tar lotion should be used as a wet dressing, and when the eruption has dried the lotion may be replaced by a 1 per cent. tar paste. Crude tar may finally be used, and may be applied to large areas of skin, for it is unusual to find infants suffering from infantile eczema intolerant to tar.

**Besnier's Prurigo.**—By this term is meant the chronic recurrent eczema which develops in childhood and adolescence often as a sequel to infantile eczema, and which affects the flexures of the knees and elbows, the forehead and the sides of the neck. In some cases it develops imperceptibly from an infantile eczema, and it is the type of skin eruption which is associated with asthma. Skin tests and elimination diets have proved most disappointing in the investigation of such cases. Occasionally the eruption has been shown to be due to contact substances such as hair, fur, flock or feathers, but in the majority of cases the cause remains as much a mystery as the cause of the asthma which so often accompanies the skin eruption or alternates with it. A definite and striking feature of the condition is the well-marked nervous irritability and suppressed anxiety which is exhibited by many of the patients. In addition to this nervous element, the skin has the capacity to develop eczema if it is scratched.

Local treatment resolves itself into the application of crude tar as soon as the state of the eruption will permit, and this must be continued for a number of weeks until the maximum thinning of the affected skin has been obtained. It is hardly ever possible to bring the skin completely back to a normal texture if the disease has been present for any length of time. X-ray treatment is almost always successful in reducing the irritation and scratching, and it may be used from time to time. It must not be forgotten, however, that these patients have recurrences over a period of years, so that there is a limit to X-ray therapy on account of the cutaneous atrophy which would result if X-rays were depended on for the alleviation of every attack.

Non-specific desensitization methods may be tried in an attempt to prevent recurrence, but the results of this treatment are not encouraging.

An individual suffering from this type of skin eruption should lead as regular and quiet a life as possible, because overwork, worry, lack of sleep and dietary indiscretions predispose to recurrence (see *Asthma*, p. 756). Change of climate or a change of locality is sometimes followed by relief, and it is remarkable how rapidly an acute exacerbation will subside if the patient is hospitalized.

Eczema due to toxic states comparable to those found or envisaged in "rheumatism" is seen to occur with increasing frequency as age advances after middle life. The eruption may be widespread or localized, and is characterized by its extreme itchiness and tendency to exacerbations and remissions. The treatment is no different from that of Besnier's prurigo, but the response to it is much more satisfactory. Free elimination is particularly beneficial, and, when the eruption is chronic and localized, X-rays are more useful than in any other form of dermatitis.

#### VARICOSE ECZEMA

When varicosity of the cutaneous venules of the legs has become established, the affected area is particularly prone to develop either chemical or infective eczema. Treatment is hampered by the inefficient circulation,

and the usual methods of dealing with these types of eruption must be supplemented in the majority of cases by rest in the horizontal position. Complicating ulceration is treated by wet dressings applied to the actual ulcer, a 1 per cent. ichthyol paste being applied to the surrounding skin. Adhesive plaster dressings should not be used when eczema accompanies ulceration.

Varicose eczema, when it heals, leaves the skin stretched, glazed and pigmented, and the recurrence which tends to take place when the patient starts to walk about can sometimes be avoided by the use of Unna's zinc ichthyol gelatin. Sometimes it may be necessary to resort to ligation of the veins in order to prevent recurrence.

### OCCUPATIONAL DERMATITIS

Eczema and simple dermatitis directly due to the individual's occupation are becoming increasingly common, and such cases often take a very long time to heal, even when the extent of the eruption is limited. They may be due to chemical irritation or to mechanical or caustic injury with dust or liquids, which allows infection to gain access to the deeper layers of the epidermis with the production of an infective dermatitis. In any case, whether due to external chemical irritation or bacterial infection, internal toxic factors may commence to play a part in the production of the rash, thus prolonging its course and increasing its resistance to treatment. All these factors must be taken into account when deciding the line of treatment to be adopted. When a case has been cured, the question of returning to work and the risk of recurrence must be considered. The individual should be warned to take every possible precaution to avoid prolonged contact with dust or liquids and to avoid all forms of minute injury to his skin. The skin should be kept as clean as possible, and emollients, such as cold cream, mixtures of lanolin and vaseline, or glycerin and water, should be used regularly after washing. No strong soaps or grease solvents should be used for cleansing purposes.

After an attack of occupational dermatitis has subsided it is wise to keep the individual off work for a period of one to two months in order to allow the previously inflamed skin to return as far as possible to normal and to recover from the effects of previous long-continued inflammation. Recurrence is practically certain when the eruption has been caused by a chemical irritant acting on a skin which is highly sensitive to it, and in these circumstances return to the employment in which the condition was acquired may be impossible.

### GENERALIZED (EXFOLIATIVE) DERMATITIS

A number of superficial inflammatory skin eruptions, which normally occur as discrete patches, may spread to involve the entire body surface. The clinical picture so produced is referred to as generalized exfoliative dermatitis. It may result from the gradual extension of any one of the types of eczema mentioned above, in which case it assumes the characteristic features of the initial patches of the disease. Psoriasis involving the whole body is frequently mistaken for generalized exfoliative dermatitis. Generalized dermatitis, which may or may not go through an exudative phase, may

follow the administration of organic arsenicals, mercury, gold and other heavy metals. A similar condition may accompany, or even precede, blood diseases of the leukæmic type and mycosis fungoides. Rarely, cases of generalized pemphigus are seen. It is possible to differentiate the various types from the clinical appearances, the history, particularly with regard to the mode of onset, and, in the leukæmic type, by a hæmatological examination.

The patient must be kept in bed for his own comfort and to permit of efficient treatment. The danger of broncho-pneumonia, due to disturbance of the heat-regulating mechanism, the result of the cutaneous vasodilatation, has been somewhat exaggerated. The treatment has already been outlined in the preceding paragraphs dealing with the different types of eczema. Dermatitis due to the internal administration of arsenic or other heavy metals is treated in the same way as that due to external chemical irritants (see p. 180). The treatment of arsenical dermatitis is also discussed on p. 216. Generalized psoriasis is dealt with in the same way as for an individual patch of the disease. The generalized leukæmic erythrodermias are intensely itchy, and tar preparations and superficial X-ray therapy are necessary. In all these cases the dressings are extensive and time-consuming, and the disease is likely to be of long duration. From time to time the patients develop diarrhoea associated with a mild fever, and tend to become emaciated and cachectic. Appropriate measures must be taken to alleviate these symptoms.

## PRURITUS

Pruritus is a sensation which is only experienced in the skin, and we are entirely ignorant of its cause. It may accompany a local pathological change which is in its essential structure similar in detail to a condition which is not associated with pruritus. Again, it is not infrequently observed that the same disease may cause intense pruritus in one patient but not in another. Itching is rarely continuous, and as a rule it comes in spasms at intervals of one to many hours, often without any apparent precipitating cause. Like the skin diseases with which it is associated, it can be profoundly influenced by external applications so that its point of origin is presumably superficial.

Pruritus occurs most commonly in conjunction with visible pathological changes in the skin. It may, however, arise spontaneously in areas of skin having a normal appearance and texture, and it is then presumably due to the action of some internal irritant on the cutaneous nerve endings, to some irritant acting reflexly on these, or to central nervous causes.

Pruritus associated with obvious skin disease is most intense at the onset of the eruption, or just prior to an exacerbation. It is usually alleviated when the disease itself begins to subside, and the treatment of the disease is the treatment of the pruritus. Thus in parasitic, bacterial or fungus infections antiseptics are used, in inflammation due to chemical irritation protective and cooling measures usually suffice, and in conditions due to some internal poison the removal of its source combined with free elimination affords relief. It is sometimes necessary, in addition to such lines of treatment, to employ specific measures to relieve the itching, which, on account of the scratching it causes, may be a serious obstacle

in the treatment of the condition responsible for it. The symptomatic treatment is limited to the application of lotions or pastes containing tar, with or without the addition of 1 per cent. phenol or menthol. Such applications are made frequently, and whenever possible the parts should be guarded from friction and changes in temperature. Exposure to X-rays is sometimes helpful. In severe cases there is no objection to the administration of sedatives of the basal hypnotic class. Morphine and its derivatives should be avoided because they have a tendency to aggravate an itch after affording initial relief. The antihistamine drugs (see p. 96) have a marked effect in relieving pruritus whether associated with an eruption or occurring in an otherwise normal skin. Following their successful administration existing itching is relieved in about twenty minutes, and by repeating the dose four-hourly it may be possible to prevent the development of further attacks. This action is most certain in urticaria, but antihistamines may be equally useful in widely differing itchy eruptions. There is, however, no criterion as to whether or not they will be effective in a given case. The preparations, dosage and toxic effects of antihistamines are discussed on p. 96. Apart from obvious disease of the skin, generalized pruritus is usually seen as an isolated symptom in elderly subjects due to some internal disorder or toxæmia. A careful examination is therefore necessary in every case to discover if possible any such factor, and its rectification is usually followed by disappearance of the pruritus.

The pruritus of the elderly is frequently associated with slight atrophy of the skin, and thorough lubrication with grease or creams, along with a liberal supply of vitamins and attention to elimination by kidneys and bowel, usually brings about a cure. Here, again, X-ray exposures may be given for troublesome areas, and sparking with a high-frequency current, using a flat glass electrode, may be helpful. It is important to avoid sudden changes of skin temperature, and all garments worn next the skin must be smooth in texture. The diet must be of an easily digestible type and all spices and condiments should be forbidden. Measures should be taken to rectify any digestive errors. Hot fluids should be allowed to cool before drinking, and it is preferable to forbid alcohol.

A few cases of pruritus are met with in hysterical young women and in both men and women under middle age, associated with some definite or incipient mental disorder, including that brought about by a drug habit.

The treatment of the pruritus so commonly met with in obstructive jaundice is discussed on p. 99.

Pruritus without any accompanying skin change may occur on localized areas, and the sites most commonly affected are the peri-anal region, the scrotum and the vulva. In such cases it is important to exclude the presence of any systemic disorder, and also to examine the immediate surroundings of the affected areas for any abnormality which might, by causing reflex nervous impulses, produce the itching. Psychological factors should not be overlooked in cases which are resistant to treatment. Any local abnormality, such as piles or enlargement of the prostate, should be dealt with. In cases of pruritus ani the bowel should be washed out, because overloading of the rectum or pelvic colon may, by causing slight peri-anal venous congestion, produce the symptom. The stools may have to be examined bacteriologically and chemically, and any abnormality rectified



by dietary measures or lavage. In cases of pruritus vulvæ the patient may have to undergo a thorough gynecological as well as a general medical examination.

The prolonged scratching associated with localized pruritus eventually leads to hypertrophy of the skin of the affected area.

The local treatment of this type of pruritus is similar to that outlined above.

Pruritus, whether localized or generalized, presents a much greater therapeutic problem when it is an isolated symptom than when it accompanies some visible cutaneous manifestation.

## URTICARIA

The majority of cases of urticaria are due to intolerance to some article of diet. The eruption occurs suddenly in an acute form, and the cause is often indicated by the history. A drastic purge and a light diet are usually sufficient to clear the eruption in the course of a day or two. Local treatment is limited to the application of an antipruritic lead and tar lotion, and the existing eruption can almost always be made to disappear rapidly by the injection of from 0.5 to 1 c.c. liq. adrenaline hydrochlor. The antihistamine drugs (see p. 96) given three or four times daily usually have a dramatic effect in relieving urticaria and in preventing further attacks. The action of antihistamines is, however, purely symptomatic, and when withheld the eruption recurs unless spontaneous desensitization has taken place. Cases of urticaria which have persisted for weeks or months may be difficult to prevent as the cause is often never determined. In dealing with such cases a series of simple diets similar to those recommended for certain cases of asthma (see p. 761) may be given to eliminate the possibility of food being the cause, and if necessary a period of starvation may be advised as an aid to dietary investigation. While these elimination diets seldom reveal the responsible allergen, the strict regimen involved not infrequently has a beneficial effect. Areas of focal sepsis must be sought and dealt with if present. Free elimination must be encouraged by diuretics and an adequate supply of fluids, and colon lavage should be carried out every second day over a period of two weeks. If no cause is discovered, non-specific desensitization may be attempted by a course of peptone injections, or by autohæmotherapy (see p. 763). Ephedrine is often useful, and in a few cases calcium administered by mouth is of service. A mixture containing pepsin and hydrochloric acid may be prescribed and will occasionally give relief, but when we are driven back upon such measures therapy has assumed a "hit or miss" aspect. It must be remembered that a certain number of chronic urticarias are really cases of dermatographism for which little can be done, although they occasionally respond to alterations in diet even although the skin eruption is not dependent on the ingestion of any particular food. Every now and then a case of urticaria is met with which seems to be due definitely to nervous influences, but this type, like that due to heat and cold, is extremely rare.

Cutaneous scratch tests with foreign proteins seldom provide any evidence which cannot be obtained by the more direct means of history taking, a complete physical examination and the results of therapy. The tests are

tedious to carry out, often extremely difficult to interpret, and positive reactions may have no relation to the case. Occasionally they demonstrate rapidly the protein to which an intolerance has been developed, but whatever indication is given by the tests it must be verified by therapy, and frequently the results of therapy do not correspond to the results of the test.

Specific desensitization to a protein which is definitely the cause of the eruption is not worth while. It is highly improbable that specific desensitization can be achieved, although over a period of years desensitization may occur naturally and spontaneously.

## DRUG ERUPTIONS

These, including enema rashes, are by no means uncommon. The majority of them do not itch, so that no treatment is required beyond the discontinuance of the causative drug. Morphine and its derivatives, however, can cause a very irritable type of erythematous and urticarial rash which may require the application of a lead and tar or a 1 per cent. carbolic lotion to allay the itching. The rashes due to the organic arsenical compounds or to gold run a very prolonged course, and their treatment has been discussed elsewhere (see pp. 216, 812).

## BULLOUS ERUPTIONS

These include dermatitis herpetiformis, the pemphigoid eruptions, iodide eruptions and certain forms of insect bites. In all cases it is advisable to snip the roofs of the bullæ and to use starch poultices until the exudative phase of the lesion has subsided. Starch poultices have the advantage that they are easily applied, and no special cleansing procedures are necessary after their removal. In addition they absorb exudate better than any other type of application. Once exudation has subsided a 1 per cent. ichthyol or ammoniated mercury paste may be applied in the form of spreads.

## HERPES SIMPLEX

At the commencement of an attack, dabbing the irritable tingling area of skin with 5 per cent. silver nitrate in spirit of nitrous ether is often sufficient to prevent the further development of the lesions. Unfortunately this treatment produces a black stain on the skin, and as the eruption almost always affects an exposed area it may not be feasible to carry it out in every case. After the eruption has developed a 1 per cent. ammoniated mercury paste is the most suitable application, and should be continued until the crusts have separated. Such treatment will undoubtedly shorten the course of the eruption. There is no method of preventing recurrences with certainty, but sparking the area of skin which is the usual site of the eruption with a high frequency current, using a flat glass electrode, may prevent further attacks. Vaccination with calf lymph as for smallpox, and also cutaneous vaccination with the fluid obtained from the early vesicles of herpes, seems to stop the recurrences in some instances.

## HERPES ZOSTER

In the early stages of this condition the injection of pituitrin is extremely useful, both in allaying the pain and in shortening the duration of the eruption. Doses of  $\frac{1}{2}$  to 1 c.c. can be given once or twice daily for the first two or three days. The affected skin should be powdered with talc and covered with a thick layer of cotton-wool. When crusting has occurred, a 1 per cent. ammoniated mercury paste can be substituted for the talc. In herpes zoster affecting the first division of the fifth nerve, great care must be taken of the eye. If lesions develop on the conjunctiva or lids, cold compresses should be used for a day or two and atropine instillations given daily. In ophthalmic zoster involvement of the conjunctiva may not occur until five or six days after the onset of the skin lesions. The after-pain of herpes zoster is treated with the usual methods suitable for neuritis.

## ALOPECIA

The treatment of alopecia depends on the cause of the condition. That following febrile illnesses or traumatic shock requires no treatment, as the hair grows in normally in due course. Patches of alopecia due to scar formation from whatever cause are permanent and no treatment is of any avail. In alopecia seen in the early stages of syphilis the hair grows in naturally, but regrowth is accelerated by antisypilitic treatment. The only forms of baldness which definitely benefit from treatment are alopecia areata and alopecia due to deficiency of thyroid secretion.

In alopecia areata counter-irritation either with chemical applications or with ultra-violet light may limit the disease and accelerate regrowth. The following lotion is widely used:—

R $\gamma$	Acid. Lact. . . . .	fl. dr. 6 (22 c.c.)
	Ol. Ricin. . . . .	fl. dr. 3 (11 c.c.)
	Sp. Meth. Indust. . . . .	ad fl. oz. 6 (170 c.c.)

Painting the patches with tincture of iodine or liquid carbolic acid is always useful and may be carried out once weekly. Ultra-violet light may be tried, using a mercury vapour lamp. Short courses lasting over a period of from four to six weeks, giving an erythema dose twice weekly, are as efficient and less tedious to the patient than a prolonged continuous course lasting for several months. Such short courses can be given at intervals of two months. In addition to local treatment, small doses of thyroid and a liberal supply of all the vitamins may be given for their properties as general growth stimulants. Attention to the general health and removal of all septic foci should, of course, be considered in addition to the local measures.

## PITYRIASIS ROSEA

This condition is self-limiting, and if it does not cause any discomfort it may be left untreated and allowed to disappear spontaneously. There is no doubt, however, that a daily potassium permanganate bath followed by the application of a 2 per cent. sulphur and salicylic acid vaseline greatly

accelerates the disappearance of the rash. If there is much irritation a 1 or 2 per cent. tar paste may be used in preference to the salicylic vaseline. Most cases will clear up quickly under the influence of one or two erythema doses of ultra-violet light, but as there is often a certain amount of irritation produced by this treatment, it is questionable if it serves any useful purpose. Pityriasis rosea seems to produce a lasting immunity and recurrences are practically unknown.

## LICHEN PLANUS

Nothing is known regarding the ætiology of lichen planus, although it has all the characteristics of an eruption due to internal toxic causes, and in addition to this it seems to have some curious association with the nervous system. In treatment one has to combat the itch, which may be intense, with suitable anti-pruritic lotions such as a lead and tar lotion, with or without the addition of 1 to 2 per cent. phenol, or the application of 1 to 5 per cent. tar paste. If the eruption is localized a full skin dose of X-rays will almost invariably relieve the itching and cause the rapid absorption of the lesions. X-rays are, of course, not practicable in extensive eruptions involving a large area of the skin surface, and their use in widespread cases has to be carefully judged. For some unknown reason, radiation of the spinal cord with X-rays relieves itching in a large proportion of cases and also causes the eruption to disappear with moderate rapidity. The area of the spine to be treated is that which gives rise to the nerves going to the area of skin affected with the rash.

Internal treatment consists in the administration of perchloride of mercury in doses of  $\frac{1}{16}$  gr. (3.2 mg.) three times daily. Arsenic is also useful, and intramuscular injections of enesol, a preparation containing mercury and salicylarsonate, have recently been found to give good results. In cases which are very resistant to treatment and in which the irritation is severe, lumbar puncture and the withdrawal of 10 to 20 c.c. cerebrospinal fluid may be followed by symptomatic relief.

## PSORIASIS

Success in treatment in psoriasis depends to a large extent on how much time a patient is willing to devote to the cure of the attack, and how much inconvenience he is willing to undergo during the treatment. Any attack of psoriasis can be cured if a patient will give up his whole time to it, and but for the fact that recurrence is almost invariable, it would be as satisfactory to treat as any other disease. In giving advice to a patient about the treatment of his psoriasis it is necessary to consider whether the amount of eruption present is sufficient to justify putting him to considerable inconvenience and expense, bearing in mind the fact that recurrence will almost always take place. This problem does not arise if a patient insists that he must be made spotless, nor when the eruption is so extensive as to cause a great deal of inconvenience from scaling, cracking and general discomfort. The treatment which will be described applies to psoriasis no matter how scanty or how extensive the eruption, and in addition to this a modified ambulatory treatment will be outlined.

**External Treatment.**—The treatment should commence with twice daily applications of a 1 per cent. tar paste, and the strength of the tar should be increased at intervals of two days up to 5 per cent. ; the increase might be graded 1, 3, 5 per cent. The tar pastes should be spread on calico. Thereafter a 5 per cent. chrysarobin paste should be applied twice daily, and it may also be spread on strips of calico or merely rubbed into the skin. When it is found that the skin will tolerate chrysarobin, and very few patients suffering from psoriasis seem to be intolerant to it, Dreuw's ointment can be used.

This should be rubbed in twice daily and should not be applied spread on strips unless to localized hypertrophic patches. If spread on strips and bandaged on, there is a very definite risk of blistering due to the high percentage of salicylic acid present in the preparation. Dreuw's ointment causes a blackish-brown discoloration of the skin, and it is superfluous to continue when a thick blackened surface layer has been formed. It is then an advantage to interrupt the treatment for two or three days and to use an ichthyol paste; first, to allow the removal of the black surface skin, and secondly, to give the patient relief from the heat and irritation which almost always accompanies the application of this preparation. The Dreuw's ointment, alternating with the ichthyol paste, is continued until the whole skin surface has become smooth and only staining marks the site of the psoriasis lesions. It is an advantage to give a week or ten days' treatment with crude gasworks tar after the Dreuw's ointment has been discontinued, because if this is done there is less chance of recurrence at an early date. Dreuw's ointment and 5 per cent. chrysarobin paste can be applied to the scalp provided it is kept shaved, and provided the chrysarobin applications are washed off at night and replaced with tar paste. There are two possible dangers associated with the application of chrysarobin, one being the production of conjunctivitis, the other, the occurrence of an erythematous and later a vesicular dermatitis. Provided the treatment is carefully supervised, the onset of either of these complications need not be considered a serious matter. The conjunctivitis can be treated with instillations of castor oil, and the dermatitis will settle very quickly after the chrysarobin is removed with olive oil, and a 1 per cent. ichthyol paste substituted. Another drawback to chrysarobin treatment of which the patient must be warned is staining of bedding, clothing and the bath. A bath need only be given every second or third day when chrysarobin is being used, and care must be taken to clean the bath immediately after use, particularly when the strong applications are being used.

If psoriasis is not treated in the fairly drastic manner outlined above, a longer period of treatment will be required. The same sequence of treatment can be employed in ambulatory patients, but in them it is only applied at night, a bath being taken in the morning, and no application made during the day.

Short of drastic treatment carried out at least once daily it seems barely worth while to advise less active methods, for they rarely meet with much success. Clothing is ruined, and the patient frequently becomes disheartened and stops all treatment. In view of this some sufferers from a mild attack of psoriasis, which is not causing any inconvenience, may be advised merely to apply a tar paste, or even plain vaseline, one or two nights weekly, and to take a bath the following morning. This type of treatment need only be considered as a toilet procedure designed to keep

the patches supple and in a state which is not troublesome. There is justification for the attitude that psoriasis is such a chronic skin affection that as little attention as possible need be paid to it unless it becomes so severe as to interfere with æsthetic feelings and personal comfort.

Recurrences take place in a most erratic way. Sometimes only a few weeks of freedom follows the complete cure of an attack, and sometimes the eruption does not recur for years.

In generalized psoriasis it may be necessary to begin treatment with plain vaseline or an ichthyol paste, and then work on to the tar pastes and finally to chrysarobin. For patients who show intolerance to tar or chrysarobin or to both, a 2 or 3 per cent. paste of oxidized pyrogallie acid, or a similar concentration of resorcin, or ammoniated mercury, may be used.

Chronic isolated patches which are resistant to local treatment, and also psoriasis affecting the nail folds, may be treated with X-rays, but, as in the case of Besnier's prurigo, the X-rays must never be repeated indiscriminately. Medicated baths have no advantages over ordinary baths.

**Internal Treatment.**—As in the case of external treatment, a large number of drugs have been advocated from time to time in the internal treatment of psoriasis, but there are only three which are of proved value, namely, salicin and salicylates, arsenic, and thyroid.

Stated briefly, salicin and salicylates—10 gr. (0.6 gm.) of each three times a day—are given in a spreading case, 3 to 5 minims (0.2 to 0.3 c.c.) of liquor arsenicals three times a day in chronic stationary cases and in those which are responding to local treatment satisfactorily, and  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) of thyroid daily to psoriatics past middle age. Various forms of diet have been advocated from time to time, but there is no one diet which is of universal help in psoriasis, and diet need hardly be considered as an aid to treatment. There is no doubt that alcohol is contraindicated when psoriasis is spreading.

G. H. PERCIVAL.

# VENEREAL DISEASES

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## THE PREVENTION AND CONTROL OF VENEREAL DISEASES (NATIONAL AND INTERNATIONAL)

**T**HE first essential in the control of venereal diseases is that there should be a national plan assuring the provision of free and confidential treatment for all sufferers from these diseases. In Great Britain this essential has been ensured since the directive to local authorities contained in the V.D. Regulations of 1916 brought about the establishment all over the country of laboratories and clinics equipped with facilities for carrying out the best available methods in diagnosis and treatment, and offering these facilities free of all charge to medical practitioners and to their patients. In addition, the Regulations of 1916 established the principle that provision should be made by the local authorities for efforts to disseminate information about venereal diseases so as to bring about the active co-operation of the public in a nation-wide drive against the spread of these infections.

By 1939, in Scotland, as a result of these measures, the annual number of cases of syphilis in the clinics had fallen to three-fifths of the number reported in 1922, and, of the total number recorded in 1939, the majority were cases of late syphilis, the recent new infections of early syphilis having declined in a much greater proportion, probably to less than one-third of those in the years following the first world war in 1914-1918. As happened in the first world war, during the second world war of 1939-1945 the number of new infections of both syphilis and gonorrhœa again underwent a very great increase. Since the later months of 1945, the return of demobilized men and women has caused a sharp upward rise in the number of fresh infections.

Owing to the increase in rapidity and in volume of intercommunication between the nations, venereal disease control must now operate throughout the whole world. Much time will elapse before the less highly organized countries attain to anything like the measure of success which, before 1939, had been achieved in Britain, the Scandinavian countries, the British Commonwealth and the U.S.A. In the Far East, in the Mediterranean countries and on the Continent of Europe there is now a vast reservoir of venereal disease which will surely overflow into countries where the standard of control is higher.

No country can now be content with an isolationist policy in V.D. control. The nations must co-operate to ensure that the advance is world-wide. International co-operation would certainly achieve the extension and development of such measures as the Brussels agreement of 1924 which provided for international reciprocity in the treatment of seamen; or the provision of bureaux, like those of the League of Nations, combating

prostitution and licensed brothels; or organizations, like the health section of U.N.R.R.A., controlling communicable diseases among displaced persons during post-war repatriation. But, so long as there is, as at present in most countries, such a low standard of sexual morality, so long will there be a vice racket, more or less conscious and organized, a Black Market in sex, with, inevitably, the persistence of conditions favouring the spread of venereal disease. The fight against venereal disease should aim at securing control over all those elements in society which, overtly or covertly, wittingly or unwittingly, derive financial gain from the exploitation of lust. The magnitude and the difficulties of such a campaign need no emphasis: those responsible for the hot-beds of infection seek the shelter and protection of powerful vested interests. Potentially infectious individuals tend to frequent certain public houses, restaurants, hotel lounges, dance halls, night clubs, and certain streets, lodging-houses, and so on. The active operation of Defence Regulation 33B, which gave power to enforce under penalty the examination and treatment of persons named as their source of infection by two patients found to be infected, frequently yielded sufficient information for the identification of sexually promiscuous persons, consorts and contacts, who spread venereal disease and who, quite often, were ignorant of the fact that they themselves were "carriers" and needed treatment. The discovery of persons who have syphilis or gonorrhœa and the application of treatment to them so as to prevent the spread of infection to others are the most practicable and effective procedures for the protection of the community. Subsidiary procedures include the application of Wassermann blood-testing on a massive scale. By the adoption of such measures, as by the spread of health education, there will gradually be created among the peoples of the world a general awareness of the value of V.D. control in promoting health, both physical and moral.

### PERSONAL PROPHYLAXIS

The opportunities afforded during the war for the close observation of controlled experiments carried out with large groups added considerably to our knowledge of the value of methods used for the protection of the individual against V.D. before, during and soon after exposure to infection. But this new knowledge did nothing to disturb the conviction that chastity and continence are still the best preventives.

For those who will accept it, the proper use of the condom (*i.e.*, no unprotected contact before or after its application; cleanliness in removal; precautions, such as lubrication, against breakage) affords a considerable degree of security. But its limitations, including the liability of unprotected parts like the root of the penis to come in contact with very fluid infectious exudates, are such that confidence in its power to protect is often betrayed. Moreover, the condom itself is frequently rejected as an irritating and intolerable obstacle by those for whom pleasure at all costs is the impelling motive.

The passing of urine in gushes followed by meticulously thorough washing with soap and water and, in women, douching, if carried out immediately after coitus, will in many cases mechanically remove all transferred infectious material before the gonococcus or the spirochæte succeed in establishing



themselves in the tissues. These elementary precautions may fail in those who have not been instructed to pay particular attention to such places as the sides of the frenum in men or the clitoris or the navicular fossa in women. Frequent causes of failure in men are phimosis or hypospadias, and, in women, the onset of menstruation and the omission of douching.

The issue of prophylactic packets was carried out on a large scale, especially in the U.S. Army. Up to about 1943 the standard U.S. Army "pro-kit" contained a cloth impregnated with soap and separate tubes of silver picrate and calomel ointments. After the latest U.S. Army individual "pro-kit" had only one tube containing combined sulphathiazole and calomel ointment. The U.S. soldiers were fully instructed and urged to report for complete "station prophylaxis" on their return to camp. The complete "station" ritual consisted of thorough cleansing with soap and water, the instillation per urethram of mild silver protein (argyrol 5 c.c. of 5 per cent. solution) and its retention for 5 minutes, followed by the inunction of 2-4 gm. of calomel ointment. In some instances, notably in the Caribbean area, for additional security against gonorrhœa and chancroid, a single dose of 2 gm. of sulphathiazole was administered by mouth. Those soldiers who used multiple prophylactic measures had an average infection rate of 0.07 per cent., an extremely low figure for a tropical theatre.

With regard to the value of "station prophylaxis," the following statement summarizing U.S. Army experience may be accepted as representing authoritative opinion:—"Chemical prophylaxis administered at a fixed station, on which great reliance has been placed in theory and in past practice, has been difficult to popularize in this emergency because of the frequent inaccessibility of stations, the time consumed in administering treatment, the messiness, occasional discomfort and lack of privacy." As the conditions of civilian life are likely to be still less favourable for any form of prophylaxis involving the supervision and ministrations of an attendant, descriptions of detailed technique for both sexes have been omitted as unnecessary.

It has been recorded that experience in the U.S. Army afforded "strong reasons to believe" that the condom had been "the most valuable single venereal disease preventive measure, as evidenced by the extent of its utilization." It has also been suggested that the capture by the Eighth Army of five million condoms taken from the Italians was of material value in protecting our troops against venereal disease while they were in North Africa.

The American Army single-tube chemical prophylactic was evolved in 1943 after considerable experimentation. The prophylactic ointment issued eventually contained "15 per cent. sulphathiazole, 30 per cent. calomel, 40 per cent. petrolatum, 14 per cent. light mineral oil, and 1 per cent. cetyl alcohol." It is claimed that "the entire procedure required only several minutes, was acceptable cosmetically, was unaccompanied by discomfort, and was easily self-administered." This preparation was specially designed to be effective against all the three important venereal diseases, *viz.*, syphilis, gonorrhœa and chancroid. One result of this extensive experience in the U.S. Services has been to advocate the adoption of a cheap and good "pro-kit" for use in civilian life.

## GONORRHOEA

The first consideration in the treatment of gonorrhœa is to make sure of the diagnosis. Verification of the diagnosis need not entail any delay in starting treatment. There are many conditions besides gonorrhœa which may cause disturbances of urinary function and which may be associated with a urethral discharge. Therefore the diagnosis of gonorrhœa should always be established and never presumed, and the simplest and speediest method of establishing the diagnosis is, whenever practicable, to demonstrate the gonococcus in a smear of purulent discharge, or in smears of the secretion from the parts liable to be affected. If in such a smear Gram-negative diplococci are demonstrated having the morphology of gonococci and occupying the intracellular position in the pus cells, then for clinical purposes it may usually be accepted that the diagnosis has been satisfactorily established. If, however, there is a possibility of legal action being taken, and where the medical examination may have to form the foundation for statements made in court and under oath, cultures should invariably be made in addition to smears, and the identity of the gonococcus proved beyond doubt by the nature of its biological reactions as well as by its morphology and Gram-negative staining. Cultures should therefore be made in the following cases:—

1. in young girls under 16 where there is an allegation or suggestion of criminal assault or indecent behaviour;
2. in cases of ophthalmia neonatorum of obscure origin where, if the gonococcus be present, the parents may be asked to submit to examination and may resent the implication that they are infected with gonorrhœa;
3. in a husband or wife where the other partner in the marriage has no symptoms and where extramarital coitus is denied;
4. in cases of proctitis where a criminal charge of sodomy may be preferred;
5. in chronic cases, *e.g.*, urethritis or prostatitis in a man, or bartholinitis or cervicitis in a woman, where the gonococci may be few and may not be found in smears unless prolonged examination be made of several specimens.

The essential preliminary to treatment, then, is in every case to make smears which may either be examined forthwith after staining by Jensen's modification of the Gram technique, or which may be sent to a laboratory after drying in air and fixing by flaming. Cultures need particular care, or else no growth will be obtained and the test will prove misleading. It is essential that the culture media should be fresh and moist and kept at body temperature both before and after inoculation.

In subacute or chronic cases, the patient should not have passed urine for 2-4 hours, and smears or cultures made first thing in the morning before the patient has passed the overnight urine give the best chance of finding the gonococcus.

In men a frequently encountered obstacle impeding an easy diagnosis is the presence of phimosis. A patient may be encountered with a tight foreskin which has become inflamed and swollen, and with purulent discharge being extruded from the small orifice of the prepuce. Such a condi-

tion may be produced by balanitis, gonorrhœa, a secondarily infected chancre, chancroid, sub-preputial warts, or by any combination of these. The swollen prepuce may be so tender as to make it difficult or impossible to retract it sufficiently to expose the urethral meatus. Under these circumstances a smear made of the discharge from the preputial orifice may be misleading, and it may be necessary to cleanse the sub-preputial sac with saline (see under Balanitis, p. 202). After cleansing and freeing the blocked preputial orifice, it may be possible to expose and take a smear from the urinary meatus or from the centrifuged urinary deposit.

In women, the chief obstacle likely to be encountered in making the diagnosis may be the menstrual period. But even when the flow is profuse it may be possible to obtain discharge or secretion from the urethra after cleansing the urethral meatus by dry swabbing or with warm saline. Smears from the canal of the cervix uteri are made by using a Graves's type of two-bladed speculum and, in subacute and chronic cases, are best taken during the increased mucous flow at the end of a menstrual period.

To take it for granted that a discharge from the genitals together with dysuria warrant an assumption of gonorrhœa and to prescribe a sulphonamide or give injections of penicillin on this assumption is greatly to be deprecated, and may lead to serious difficulties. It is unjustifiable to let a husband or a wife go on worrying about gonorrhœa when the discharge and pain on micturition are really caused by a non-gonococcal (*e.g.*, staphylococcal) urethritis, which does not necessarily carry an implication of marital infidelity. Diagnostic tests should invariably be made, possibly to be reported on later, and then, and only then, should treatment be prescribed. It is necessary to add that, in subacute and chronic cases, one set of smears and cultures may not be sufficient: in such cases, repeated tests must be made before the possibility of obtaining a positive result can be abandoned.

The diagnostic examination should be completed by the taking of blood for the gonococcal complement fixation and also for the Wassermann and Kahn tests. The G.C.F. test is useful in diagnosis within the limits of its validity: its application in early recent infections is limited by the fact that it may take from one to five weeks to become positive, and that a positive reaction is to a considerable degree determined by the presence or absence of a "shut-in" focus of infection.

### THE IMPLICATIONS OF A CASE OF GONORRHŒA

When the diagnosis of gonorrhœa has been securely made by the finding of gonococci in smears and cultures and when the treatment of the patient with penicillin or a sulphonamide drug has been commenced on the lines to be described, consideration should be given to the various implications inherent in the diagnosis. If the patient be married, no time should be lost in ascertaining definitely whether or not the other partner in the marriage has been, or may have been, exposed to the risk of transmission of the infection, through contact, even during the incubation period and before the first symptoms appeared. This frequently means the examination of the marital partner, and examination means explanation.

The next implication to be tackled is the question of the likely source of infection and any other contacts. This aspect should not be dismissed after a cursory mention, but pursued in a determined manner in the expecta-

tion of finding, if possible, definite names and addresses of consorts, or, at least, detailed identifying particulars which may then be transmitted to the local M.O.H. for necessary action. In dealing with this highly contagious and readily transmissible disease, the safeguarding of the health of the community is an obvious obligation, and contact tracing is the best way of discovering "carriers."

### THE HYGIENE OF THE PATIENT

The patient should be instructed in the nature of the disease, and especially in the precautions to be taken to avoid transmitting it to others. The advice to be given to the patient may be collected under the headings: (a) infectivity; (b) the disposal of the discharge and the protection of clothing; (c) food and drink; (d) work and exercise.

**Infectivity.**—The patient should be told that the infectivity resides in the discharge, and that the possibility of transmission to others can easily be prevented by reasonable precautions. He must have no sexual intercourse until told that it is safe. If possible he should have a bath every day and must keep his own sponge, soap and towel. He can keep the household bath safe by being the last person at night to use it and by washing the bath afterwards with a pint of water containing a tablespoonful of liquor chloroxylenolis (dettol). Alternatively he should wash the genital area frequently with soap and water. Hands soiled with urine or discharge should be washed at once with soap and running water. Too much need not be made of the danger of conveying infectious material to the eyes, as either sulphonamide or penicillin will prevent such a risk from materializing. The same precautions, especially twice-daily sitz baths, apply to women.

**The Disposal of the Discharge and the Protection of Underclothing.**—This is less of a problem now than it used to be, as treatment will usually stop the discharge, or, at any rate, the gonococcal element in it, in 24-48 hours. A man may protect his shirts by safety-pinning a piece of lint 1 foot square to the inside of his undervest so as to cover the penis, or by wearing a light knitted jock-strap (*e.g.*, "Litesome" pattern) to support a good-sized pad of cotton-wool for catching the discharge. The soiled lint or wool should be burned. Women may wear a sanitary pad which should be changed frequently and dusted with the zinc oxide, bismuth subgallate powder described later (see p. 206). In women, there may be some risk of a profuse discharge running back and infecting the anus. This may be avoided by keeping the part clean and by inunction with an ointment containing 5-10 per cent. of sulphathiazole. The patient should be assured that the gonococcus is easily killed by washing with soap and very hot water, and should be deterred from needlessly burning irreplaceable underclothing.

**Food and Drink.**—With penicillin or sulphonamide treatment, little change need be made in the patient's food unless there be an acute complication like a prostatic abscess or a salpingitis, when a light diet is advisable. Condiments should not be added to food. The chief restriction is on alcohol, which should be barred in any form.

**Work and Exercise.**—Now that penicillin or sulphonamide treatment is available, little or no restriction need be placed on work in early cases without complications. Acute prostatitis, epididymitis, arthritis, Bartholin's

itis or salpingitis are indications for treatment in bed. Certain activities, like cycling or horse-riding, which may traumatize the inflamed urethra, or dancing, which may induce sex-stimulation, should be avoided. Nowadays, the acute symptoms are usually cut short so quickly that little alteration in the patient's daily life is necessary. He should not be allowed to take his disease either too lightly or too seriously.

### SPECIFIC TREATMENT

**Penicillin.**—Penicillin is to be preferred to sulphonamide therapy in all cases except the following:—

- (a) where there is a concomitant ulcerative or erosive condition and specimens of serum are being taken for examination for spirochæta pallida by dark-ground illumination. In such cases penicillin used in the treatment of gonorrhœa militates against the finding of spiro. pallida;
- (b) where there is phimosis, and balanitis which may be syphilitic—for the same reason as in (a);
- (c) where the patient (*e.g.*, deep-sea merchant navy) cannot be kept under observation for concomitant syphilis;
- (d) perhaps in pregnancy because of the effect on the child of possible delayed recognition of concomitant syphilis;
- (e) in infants where testing for congenital syphilis is being carried out;
- (f) where injections are contraindicated or are objected to.

**Oral Administration.**—In Britain, penicillin for gonorrhœa is still (1947) given almost entirely by parenteral injection. It may sometimes be given orally to young babies suffering from gonococcal ophthalmia, as in very young infants the penicillin may escape destruction in the stomach and be absorbed from the alimentary tract in a therapeutically effective concentration. If suitably protected by a gastric antacid from destruction in the stomach, penicillin may be given by the oral route even to adults, but this technique has not been fully developed and therefore cannot as yet be recommended.

**Parenteral Administration.**—Parenteral penicillin may be given intramuscularly or subcutaneously either by multiple-injection technique, or by limited ("1-shot" or "2-shot") injection methods.

For *multiple injections* sodium penicillin is used, the individual dose being dissolved in 1-2 c.c. of sterile distilled water. The site of injection is the upper outer quadrant of the buttock, the two hips being used alternately. A multiple-injection technique should be chosen where there are complications, and in these cases the patient is confined to bed. As multiple injections may carry a greater assurance of cure, this method may also be preferred where economy of time and effort is of less importance. Now that supplies of penicillin are more liberal and cheaper, there is less point in trying to limit the total dose to the minimum necessary for high efficiency. Accordingly, for cases without complications an appropriate schedule would comprise 5 doses each of 50,000 units at intervals of 2 or 3 hours, the total dose being 250,000 units and the time required 8 or 12 hours. For cases

with complications, 3-hourly injections each of 50,000 or 100,000 units should be given by round-the-clock administration, 8 injections in each 24 hours, and continued for from 48 to 96 hours or longer according to the severity of the complication and the therapeutic response. Where there is a "shut-in" focus with pus formation, which may take some time to drain, or where surgical interference may be required, *e.g.*, a peri-urethral, prostatic or bartholinian abscess or a pyosalpinx, the injections should be continued for 4 to 6 days. If, in such cases, there should appear to be a possibility of delaying the recognition of a concomitant syphilis (*e.g.*, where there is phimosis with balanitis), then it is wise to increase the individual dose to 100,000 units and continue the 3-hourly injections until the patient has had a dosage sufficient to cure a very early syphilis, *viz.*, in the order of 5 million units. This procedure of giving full antisypilitic dosage seems desirable in cases where the first two or three doses are followed by a pronounced febrile reaction of the Herxheimer type which is so frequently encountered when penicillin is used for the treatment of early syphilis. No doubt a positive Wassermann and Kahn test should now declare the syphilis, but sometimes these reactions are delayed. In cases of gonococcal arthritis, the treatment should be continued for at least 6 days and preferably combined with from two to six sessions of inductopyrexia.

Techniques where the *number of injections is limited to one or two* are specially suitable for those early uncomplicated cases when it is important that the treatment should be carried out with the minimum loss of time and the minimum interruption of the patient's routine of work: they are designed for ambulatory out-patients so as to make the minimum demand on the time and effort of both patient and doctor. If circumstances should make it impossible to give more than one injection, the action of the penicillin may be prolonged by using a suspension in oil and beeswax (P.O.B.). The ordinary preparation of P.O.B. carries 125,000 units in 1 c.c. and the single dose given should be one of  $2\frac{1}{2}$  c.c. or 3 c.c., *i.e.*, 312,500 or 375,000 units. It may be possible to get a specially made preparation of P.O.B. containing 300,000 units in each 1 c.c. and therefore corresponding to the recommended Romansky formula: of this more concentrated preparation the single dose given should not be less than 1 c.c. and preferably  $1\frac{1}{2}$  c.c. For the technique of administration of P.O.B. see the section on penicillin (p. 91).

P.O.B. technique demands special care and requires much more time in preparation than is needed for the simple solution of ordinary sodium penicillin powder in sterile distilled water. Moreover, two injections of 250,000 units of sodium penicillin in aqueous solution at an interval of 4-6 hours will give a cure-rate of around 96 per cent. in uncomplicated cases. From the point of view of ease of administration and certainty of action, this is recommended as the ideal method. For the 4 per cent. of failures, cure may be achieved either by adopting a multiple-injection technique or by giving a 5-days' course of 5 grams of sulphathiazole or sulphadiazine per day (see p. 200).

The doses and courses of penicillin described are suitable for adults of both sexes. It is most unusual for the few injections required to cure uncomplicated gonorrhoea to produce any untoward effects such as local pain at the site of injection or a general allergic manifestation such as urticaria. The longer courses required for such complications as arthritis or for concomitant syphilis may, in certain sensitive individuals, give rise

to a more or less severe urticaria, and swelling, pain and tenderness in the hips. The treatment of such reactions will be discussed later (see p. 213). See also the section on antihistamine drugs (p. 99).

**Sulphonamide Therapy.**—The two best sulphonamide drugs for the treatment of gonorrhœa are sulphathiazole and sulphadiazine: of the two, sulphadiazine has the fewer toxic effects, but, so far as efficacy is concerned, there is little to choose between them. Sulphapyridine is less effective and is so liable to produce nausea that it should never be used; sulphanilamide is also less potent. Sulphathiazole or sulphadiazine should be given in a short intensive course of 5 days' duration. If it proves necessary to give a second course, an interval of 5 to 7 days should be allowed to elapse. Toxic effects from sulphonamides are much more apt to occur if the course, even in a modified form, is continued beyond 8 days. Both sulphadiazine and sulphathiazole are issued in  $\frac{1}{2}$ -gram tablets, and the normal dose is 2 tablets (1 gram) to be taken 4-hourly for 5 doses in the 24 hours. Ordinarily, if the patient is to keep at his work it is impracticable for him to take the drug during the usual hours of sleep; in practice, therefore, the patient is instructed to take 2 tablets every 4 hours during the daytime, starting at 7 a.m. or 8 a.m. and finishing at 11 p.m. or 12 midnight. If a diagnosis is made in the afternoon or evening, it is good practice to start off with one or two double doses of 4 tablets (2 grams) each, as in this way an effective blood concentration is quickly achieved. It is never necessary or advisable to prescribe more than 25 gm. for a course. The sulpha-drugs are scheduled and the prescription must bear both the patient's and the doctor's full name and address. Prominent among the instructions to be given to the patient is the need for a copious fluid intake: this may be made precise and definite by impressing on the patient that he must drink  $\frac{1}{2}$  pint of water with each dose of 2 tablets. Further details of administration are given in the section on sulphonamide therapy (see p. 71).

**Urethral Irrigations.**—In female patients, urethral irrigations are seldom required. The drainage of the short ( $1\frac{1}{2}$ " ) urethra is good, and persistence of the infection in the para-urethral crypts of Skene is best dealt with by electro-cauterization with a fine platinum wire terminal. In male patients treated either by oral sulphadiazine or parenteral penicillin, a slight thin mucopurulent, mucoid or watery discharge sometimes persists after the thick purulent discharge has stopped, as it ordinarily does in 2 or 3 days' time. A smear of such a thin residual discharge commonly shows absence of gonococci, pus cells in diminished numbers, epithelial cells in excess, and varying, but usually small, numbers of "secondary" organisms, cocci and bacilli, showing positive or negative reactions to the Jensen-Gram stain. In such cases daily irrigation for 3-6 days with a 1 in 10,000 solution of potassium permanganate (made by adding 3 drachms (10.8 c.c.) of stock 1 per cent. solution to 2 pints of warm water), or a 1 in 5,000 solution of chloramine-T. (3 drachms (10.8 c.c.) of 2 per cent. stock solution in 2 pints of warm water), frequently accelerates the disappearance of the slight discharge. Also, in male cases being treated with a sulphonamide, even if gonococci are still present in the smears, irrigation may be prescribed for 5-7 days before commencing a second course of the tablets. In general, however, in the vast majority of either penicillin- or sulphonamide-treated cases, no irrigation is required.

### THE SURVEILLANCE AND TESTING OF UNCOMPLICATED CASES

If relapse occurs after penicillin or sulphonamide therapy, it usually does so in the first week after the cessation of treatment, so it is ideal to see the patient every day or every other day for a week, and thereafter every week for another 4 weeks. The patient should be directed not to pass urine for 2-4 hours before reporting. Smears should be made of any secretion that may have gathered in the urethra, and the urine should be inspected for haziness due to pus, or for pus threads. After a week of clear urine and of freedom from symptoms, the prostate should be massaged and the seminal vesicles stripped. Usually secretion will appear at the urethral meatus and a smear of it can be made, or a smear may be made from the centrifuged deposit of the urine after the prostatic massage. The prostatic secretion should not contain more than a few scattered polymorph leucocytes and no organisms other than commensals from the navicular fossa attached to the epithelial cells. If the patient sees a urethral "bead" first thing in the morning, he should be given two glass slides and instructed how to make a thin smear on one slide by spreading the "bead" with the edge of the second slide. These morning smears should show a small and gradually diminishing pus cell content, no gonococci, and only the almost inevitable commensals.

The old prolonged irrigation treatment, especially if not skilfully applied, frequently caused irritation and aggravated the tendency of a resistant gonorrhœa to induce infiltration and cicatricial changes in the urethral lining. With the virtual abandonment of the old methods and the universal adoption of the rapidly curative penicillin and sulphonamides, the need to examine and search the urethra for evidence of infiltrations or for persistent pockets of infection has largely disappeared. There is now no need to use the urethroscope as part of the test of cure in uncomplicated cases of gonorrhœa, and it is doubtful if even the passing of straight or curved bougies is any longer really necessary in such cases. If all forms of instrumental investigation can safely be dispensed with, the relief to the mind of the average patient can well be imagined. Moreover, in the past, fear of the instruments was probably a frequent cause of failure to keep on attending for the usual 3 or 6 months' period of observation. Satisfactory and painless testing for cure can be achieved by repeated diligent examination of smears of the urethral and prostatic secretions, particularly if the urethral smears are made before the patient passes urine in the morning.

Doubts as to the reality of cure may arise if there be persistence of a slight discharge, sometimes denoted by a stickiness or gumming together of the lips of the urethral meatus, or by a persistent "morning bead," or by haziness of and "threads" in the urine. In all such cases, evidence from the smears may be supplemented by cultures, but it should be noted that cultures are useless and may even be misleading if all the precautions mentioned in the section on diagnosis (see p. 195) are not attainable or are not strictly observed.

If the original Wassermann, Kahn and gonococcal complement fixation tests are negative, they should be repeated after 1 month, and, if still negative, after 3 and 6 months. The amount of penicillin used for the treatment of a gonorrhœa is insufficient to cure a concomitant and more



slowly incubating syphilis, and may delay its recognition. Sometimes an erosion or an indurated area appears which probably represents a chancre and yet no spiro. pallida are found in dark-ground-illumination examinations of serum from the lesion, and the appearance of positivity in the Wassermann and Kahn tests may be delayed. Therefore clinical and serological observation for syphilis should be continued for 6 months, in order to allow for prolongation of the incubation period and to give time for the syphilis to be revealed in the blood tests. If the blood gonococcal complement fixation test should remain persistently positive, and this is unlikely in uncomplicated cases, an intensive search should be undertaken for a residual focus, which is most usually located in the prostate or seminal vesicles in men, or in the cervix, fallopian tubes or bartholinian glands in women.

### COMPLICATIONS OF GONORRHOEA IN MEN

The rapid and almost invariable success of penicillin justifies the drastic curtailment of this section. Even if a modern sulphonamide be the therapeutic agent employed, the curative action is usually so speedy that the infection is eliminated long before the time when complications are likely to arise. Occasionally, however, the first sign of a gonococcal infection in a man is an epididymitis.

**Balanitis and Balano-Posthitis.**—If a man with a tight foreskin gets gonorrhoea, the irritation of the discharge accumulating inside the prepuce is likely to set up an inflammation of the skin surfaces of the glans penis and of the inner aspect of the prepuce. This condition may either simulate or be associated with and mask other concomitant conditions such as chancre, chancroid, fuso-spirillary balanitis, sub-preputial warts, etc. The taking of material for diagnostic tests is hampered, and this difficulty has already been considered in the section on diagnosis (see p. 195). As long as diagnostic tests are being made, the sub-preputial sac should be irrigated (with a fine cannula inserted through the phimotic orifice and passed back to the balano-preputial fold) with warm saline only. After the diagnostic testing has been completed, a 1 in 10,000 lotion of potassium permanganate may be substituted for the saline. If the swollen prepuce be retractible, frequent bathing with warm saline or with 1 in 10,000 solution of potassium permanganate after the diagnostic period, and the introduction between the opposed skin surfaces of a thin dressing of cotton-wool moistened with saline or weak permanganate lotion, will speedily clear up the inflammation. A cream containing 10 per cent. of sodium sulphacetamide is a soothing and satisfactory dressing for these cases. Sometimes the dammed-up gonococcal discharge causes an infection of one or other of the Tyson's ducts (lying in the coronal sulcus on either side of the frenum), and abscess formation may result, necessitating aspiration or incision and drainage. After aspiration a small quantity (say  $\frac{1}{2}$  c.c.) of solution of sodium penicillin (50,000 units/c.c.) may be introduced into the cavity: meantime, parenteral penicillin is continued by multiple injections. Care should be taken to avoid the abscess or the needle penetrating into the urethra and so determining a urinary fistula.

**Peri-urethral Abscess.**—Such an abscess causes a swelling projecting from the floor of the penile urethra, often about an inch from the meatus, but sometimes further back. A peri-urethral abscess projecting into the

perineum or into the neck of the scrotum may occur where a recent gonococcal infection is superimposed on an old stricture of the urethra. Aspiration of the pus, followed by introduction into the abscess cavity of  $\frac{1}{2}$ -1 c.c. of sodium penicillin solution (50,000 units/c.c.), will usually bring about resolution. Meanwhile, parenteral penicillin is continued by a multiple-injection technique. If repeated aspiration should fail, the abscess may be incised, pus evacuated, and the cavity packed with gauze soaked in penicillin solution. A co-existent or threatened stricture will require periodical dilatation.

**Epididymitis and Vasitis.**—The patient must be kept in bed on a light diet and given either parenteral penicillin by multiple injections or a course of sulphadiazine or sulphathiazole as already described. The drag downwards of the heavy, swollen and tender scrotum and its contents should be prevented by supporting the part on a large pad of wool pulled up by a T-bandage. If the swelling be great and the pain severe, a hot dressing of kaolin poultice or a fomentation may be applied. When the acute inflammation has subsided and the urine has become clear, the usual concomitant involvement of the prostate and seminal vesicles will require investigation and treatment by twice-weekly massage controlled by the examination of smears.

**Prostatitis and Seminal Vesiculitis.**—Little need be added to what has been said above in regard to the treatment of epididymitis, *viz.*, rest in bed, a multiple-injection course of penicillin or a course of oral sulphadiazine. Abscess formation in the prostate may cause acute retention of urine, which usually requires to be relieved by catheterization with a boiled soft rubber catheter after washing out the anterior urethra with 1/5,000 chloramine-T. The passing of the rubber catheter should be facilitated by anæsthetizing the anterior urethra with 10 c.c. of a surface anæsthetic such as diluted anethaine (2 c.c. of stock 2 per cent. solution plus 8 c.c. sterile distilled water), introduced by means of a 10 c.c. all-glass Janet-pointed syringe, after washing the meatus with soap and water and cleansing with alcohol. The catheter should be lubricated with a special lubricant such as Lilly's. If this should fail, or if the patient needs catheterization more than once, he should be put under the care of a specialist, as occasionally a severe prostatic abscess may endanger life.

Acute seminal vesiculitis is generally declared by the occurrence of hæmaturia and of painful erections of the penis. As hæmaturia may also be a manifestation of intolerance to sulphonamide therapy, these cases should invariably be treated with penicillin given by multiple injections. Another source of confusion may be the occasional association of a gonococcal infection with Reiter's disease (see p. 238), so that the advice of a specialist should always be sought in these cases.

**Arthritis and Iritis.**—Prostatitis and seminal vesiculitis, acute, subacute or chronic, are not infrequently associated with metastatic complications such as arthritis and iritis. Probably the best treatment for such cases is a combination of a prolonged course of multiple-injection penicillin along with repeated hyperpyrexia induced by twice-weekly sessions in the inductotherm fever cabinet, giving at each session a spell of 3-5 hours at a temperature around 105.8° F. This necessitates admission to hospital under the care of a specialist. Short of this, fever therapy may be applied by giving the patient twice-weekly intravenous injections of T.A.B. vaccine, starting

with a dose of 25 million, then 50 million, then 100 million, and increasing by increments of 100 million to 500 million.

When the acute phase has passed and the urine becomes clear, prostatic massage should be performed twice weekly and controlled by smears until the polymorph leucocyte content of the secretion has become normal.

With penicillin therapy available, the subsidiary problems of treatment are less insistent than they used to be. Very acutely painful joints may be immobilized for a short time in splints or between sandbags, but a good range of mobility should be preserved by early passive and active movement and massage. For the control of a severe arthritis, so as to ensure speedy and complete restoration of function, the help of an orthopædist may be enlisted; and for the control of an iritis it is well to seek the advice of an ophthalmologist. In acute iritis, unless there be an increase in the intra-ocular tension, the inflamed tissue should be put at rest by dilating the pupil with a 1 per cent. solution of atropine sulphate, one or two drops being instilled night and morning. Occasionally, atropine is not well tolerated and causes conjunctivitis, and in such cases 2 per cent. homatropine may be substituted. Pain in the eye may sometimes be relieved by the application of an electrically heated pad. Iritis should always be regarded as a menacing complication: it is very prone to recur and to leave such sequelæ as anterior and posterior synechiæ adhesions to the posterior surface of the cornea or the anterior surface of the lens. These synechiæ cause the pupil to become irregular, and, through residual uveitis, the cumulative effects of recurrent attacks may eventually lead to serious and irreparable loss of vision of one or of both eyes. It is well to note that gonococcal iritis may be, and not infrequently is, aggravated by any other concomitant septic focus, particularly an alveolar abscess, which should receive appropriate treatment.

**Direct Gonococcal Infection of the Conjunctiva in Adults.**—This complication is rare, but when it does occur it responds well to multiple-injection penicillin along with local applications to the conjunctival sac of drops of 20 per cent. solution of sodium sulphacetamide. Drops made from the ordinary commercial (yellow) penicillin are apt to be irritating to the eye, and if penicillin is to be used for local application, the solution containing 2,500 units to the c.c. should be prepared from the purest crystalline penicillin G ("white penicillin"). In order to maintain an adequate concentration in the conjunctival sac, the penicillin drops must be put in the eye very frequently, *e.g.*, every minute for the first 30 minutes, after which the frequency of administration may be gradually reduced.

**Cutaneous Lesions.**—Occasionally small abscesses and sinuses form in the skin of the penis, especially of the outer surface of the prepuce. Gonococci can be demonstrated in the pus from the sinuses. Pus should be aspirated from the larger pockets and an equivalent amount of penicillin solution (50,000 units/c.c.) instilled into the cavity. Smaller pockets and sinuses may be obliterated with an electric cautery wire. Alternatively, small abscesses may be incised and their walls cauterized, or the cavity packed with gauze soaked in penicillin solution or with 5 per cent. sulphathiazole paste.

In cases of urethritis complicated by arthritis, and possibly iritis, hyperkeratotic papules may appear on the skin of the glans penis and prepuce or on the skin of the soles or elsewhere. Sometimes these papules are induced to appear by heat and moisture, *e.g.*, on the skin around a joint which has

been fomented. The lesions on the glans penis tend to present red patches with circular or semicircular margins ("balanitis circinata"). Especially on the soles, where the condition tends to be bilateral, the papules become raised and horny in the centre with a red edge, and this manifestation is called "keratoderma blenorrhagica." In patients showing these symptoms gonococci may not be found in smears of the urethral discharge and the G.C. fixation test of the blood may be negative. In spite of repeated negative findings, there was formerly a tendency to regard the association of the skin lesions, the arthritis and the iritis as being caused by metastatic gonorrhœa. It now seems likely that such cases are really examples of Reiter's disease (see p. 238), and it also seems possible that Reiter's disease and gonorrhœa may occur in association. Gonorrhœa, if present, is treated by a prolonged course or courses of multiple-injection penicillin (the individual dose being high, say 100,000 units), with the addition of fever therapy given by intravenous T.A.B. vaccine or by inductopyrexia. The skin lesions gradually clear up, as the urethritis and the arthritis subside under the general treatment.

### GONORRHOEA IN WOMEN

Gonococcal infections in women tend to be particularly severe during or shortly after a menstrual period or if the infection occurs shortly after child-birth or after a miscarriage. On the other hand, when the infection is first acquired there may be 3 or 4 days of scalding pain on micturition and frequency—symptoms which are often ascribed to "a chill on the bladder," and then the infection settles down into latency with few symptoms. There may or may not be a vaginal discharge.

Frequently gonorrhœa in women is associated with infestation of the vagina by the protozoal parasite, the trichomonas vaginalis. This infestation, if not treated *pari passu* with the gonorrhœa, will cause the persistence of a vaginal discharge after the gonorrhœa has been eradicated.

**Specific Treatment.**—Parenteral penicillin or oral sulphadiazine or sulphathiazole are applied by the same methods and in the same dosage as for men. In uncomplicated cases a high cure-rate will be achieved by a two-injection large-dose technique, *e.g.*, two doses each of 250,000 units separated by an interval of 4-6 hours. Nevertheless, at least one account has been published recently of a series of female cases in which the results achieved by penicillin, even when applied in high dosage by multiple injections for the treatment of concomitant syphilis, were extremely disappointing. The prognosis in female cases should not be too optimistic. If, after the dosage advised, clinical and/or bacteriological relapse should occur, cure may be achieved by adopting a multiple-injection technique (say 50,000-100,000 units two-hourly for 5 injections, *i.e.*, a total of 250,000 to 500,000 units), or by giving a course of sulphathiazole or sulphadiazine. The cure of gonorrhœa in women, even of uncomplicated cases, may be more difficult than in men, and tests of cure should be correspondingly even more rigorous and thorough.

If the discharge should persist after penicillin or sulphonamide treatment, this may indicate a failure to eradicate the gonococcus or the presence of trichomonas infestation or vaginal thrush (for treatment of these, see under complications).

**Vaginitis and Cervicitis, Gonococcal and Post-Gonococcal.**—In the customary treatment of vaginitis, a large part has been played by dry swabbing followed by the insufflation of a powder carrying in each ounce a drachm (3.9 gm.) of zinc oxide, two drachms (7.8 gm.) each of subgallate of bismuth and light magnesium carbonate, the vehicle making up the remainder being powdered starch. With the addition of 10 per cent. of powdered sulphathiazole, this powder may be applied locally, using a speculum to obtain access where there is evidence of a gonococcal infection of the posterior fornix of the vagina.

Just as the irrigation treatment of urethritis in the male has fallen into disuse, so also it seems likely that the day of frequent topical applications to the cervix has passed. Medicated pessaries, which had a great vogue in the past, may still occasionally be useful as pessaries carrying 10,000 units of penicillin, preferably of the pure crystalline penicillin G in a cocoa-butter base.

Recent work has tended to emphasize the relationship that exists between the bacterial content of the vagina and the vaginal pH. It has been shown that the high acidity of the normal vagina exercises a strong deterrent to the growth of pathogenic bacteria. This acidity is conditioned by the production of lactic acid from the glycogen in the epithelial cells, a process which is associated with the numbers and activity of the vaginal bacilli of Döderlein. Research has concentrated on the necessity of reproducing as nearly as possible the high acidity of the normal healthy state, and has also been directed towards devising a form of treatment which could easily be used by the patient herself at home. Judging by the results achieved, one of the best of these recent preparations is an acid jelly containing 3 per cent. lactic acid, 1 per cent. acetic acid, 0.1 per cent. sodium tetradecyl sulphate, in 85.9 per cent. polyethylene glycol, and incorporating 10 per cent. of sulphathiazole. This jelly necessitates the use of an applicator similar to that supplied with certain contraceptives. In so far as it produces conditions antagonistic to the growth of all the ordinary pathogens of the vagina, this acid jelly is calculated to produce a good response in most cases of vaginitis even in those caused by trichomonas or by thrush.

Cervical erosions are frequently hormonal in origin and dependent on ovarian activity: aggravation due to the gonococcus will be benefited by the general specific therapy with penicillin or sulphonamides, and small residual erosions do not call for treatment.

#### COMPLICATIONS OF GONORRHOEA IN WOMEN

**Trichomonal Vaginitis.**—Infestation with the flagellate protozoon, *trichomonas vaginalis*, is best diagnosed by recognizing the characteristic erratic movements of the parasite in a fresh wet preparation viewed by a  $\frac{1}{8}$ " lens with reduced illumination or by a  $\frac{1}{12}$ " oil-immersion lens and dark-field illumination. To make the preparation, a drop of the vaginal discharge may be mixed with a drop of dilute solution of safranin (red stain), 1 part of 1 per cent. safranin to 4 parts saline: the safranin dyes the cells and leaves the trichomonas unstained. Concomitant infestation with the trichomonas vaginalis is one of the commonest complications of gonorrhoea in women, and is not greatly influenced either by parenteral penicillin or by oral sulphonamide, any apparent temporary improvement being probably due to successful treatment of the associated secondary infection. The condition, however,

responds to local treatment with acetarsol, which may be applied in the form of tablets each containing 4 grains (0.24 gm.), 2 to 4 tablets being inserted high up into the vaginal fornices after first swabbing the walls with a saturated solution of sodium bicarbonate. The patient herself inserts the tablets when lying on her back in bed. At first the tablets are inserted twice daily, say for 3-4 days, then once daily, and continued during the menstrual period. The treatment is gradually reduced in frequency until it is given only on the 4-6 days immediately following the menstrual period. Trichomonal infestation is very liable to recur, but may be kept in check by the occasional use of the acid jelly described above.

**Vaginal Thrush.**—*Monilia* infections of the vagina and vulva respond well to applications of a 1 per cent. aqueous solution of gentian violet, or 1 or 2 per cent. of gentian violet may be incorporated in a jelly for local application, *e.g.*, in the acid jelly base already noted. Vaginal thrush is frequently encountered in pregnancy.

**Infection of Bartholin's Glands and their Ducts.**—Gonococcal infection of a Bartholin's gland, if untreated in the early stages, tends to go on to abscess formation. Such an abscess may be treated on much the same lines as peri-urethral abscess in the male, namely by systemic multiple-injection penicillin, supplemented by aspiration of the pus and instillation into the cavity of a corresponding amount of penicillin solution (50,000 units/c.c.). Meanwhile the parenteral penicillin is continued by 3-hourly injections, *e.g.*, 50,000 to 100,000 units 3-hourly for 3-4 days.

**Salpingitis.**—A gonococcal infection which has extended to the fallopian tubes can usually be checked by systemic multiple-injection penicillin. Large individual doses should be given, say 100,000 units 3-hourly, and maintained for 4-6 days or longer. The patient is kept in bed until the acute symptoms have all subsided and for some time afterwards, and it has been customary to keep these patients well propped up in a half-sitting position. Salpingitis is most likely to occur during menstruation or after a confinement or a miscarriage. The patient looks and feels very ill, and the condition must be discriminated from appendicitis, ectopic gestation or an ovarian cyst with twisted pedicle. If the patient has an acute cervicitis, if gonococci have been found in a smear of the cervical discharge, and if the other causes of an acute abdominal condition have been excluded, it is justifiable to adopt an expectant attitude while continuing the parenteral penicillin. Surgical intervention is contraindicated.

If not treated, an acute salpingitis tends to subside in from 10 to 14 days, becoming subacute and then chronic with such sequelæ as extensive adhesions in the pelvis involving tubes, ovaries and uterus, distorted and twisted tubes and displacements of all these organs. The result is pelvic invalidism and prolonged ill-health, and sometimes the conglomerated mass in the pelvis has to be removed by operation. A subacute or chronic focus in the tubes may determine such a metastatic complication as arthritis, and treatment for this follows the same lines as for arthritis in the male, the special indication being hyperpyrexia induced by inductothermy or intravenous T.A.B. vaccine.

#### TESTS OF CURE FOR WOMEN

As relapse is most likely to occur within the first fortnight after cessation of the penicillin or sulphonamide treatment, the patient should be seen

twice a week during this period, and a successfully treated case will show freedom from symptoms and absence of gonococci from smears of the urethral, cervical, and bartholinian gland secretions. Thereafter the patient should report after each of three successive menstruations when smears are taken from the areas of possible infection, and blood is withdrawn for the Wassermann, Kahn and gonococcal complement fixation tests. As the menstrual flow contains numerous polymorph leucocytes, the presence of these cells in cervical smears need not be interpreted as unsatisfactory provided gonococci are absent. Nevertheless, when the slightest doubt arises, smears should be supplemented with cultures. In uncomplicated cases when treatment has been begun early, the blood gonococcal complement fixation test may have been negative when first taken and remain negative throughout. Shut-in foci in the Bartholin's glands, the cervix and the fallopian tubes, and delay in starting treatment tend to cause various degrees of positivity of the G.C. fixation test. When cure has been achieved in such cases, the titre of the complement fixation test should progressively decline to negativity: failure to do so will arouse suspicion, and a resistant focus should be searched for persistently. Metastatic complications, especially arthritis, tend to be associated with a strongly positive G.C. fixation test, and the reversal of such a +++ test may take many weeks, or occasionally even months. When penicillin has been used, the Wassermann test should be applied periodically for 6 months after the treatment, in case the serological development of a concomitant syphilis should have been delayed.

#### GONORRHOEA IN LITTLE GIRLS

Female children are usually infected accidentally through contact of the vulva with pus-contaminated articles such as sheets, blankets, towels, rugs and possibly W.C. seats. As a measure of prevention, all female children sent for admission to hospital should have an examination made of the vulva for redness, increased secretion and discharge, and smears made if these signs are present, before being admitted to a ward, especially to a children's ward. Even a child so young as 6 years may show acute abdominal symptoms resembling appendicitis which are really due to a gonococcal salpingitis. The nursing of cases of gonococcal vulvo-vaginitis calls for special precautions to minimize the risk of transfer of infection, and each child should have its own personal toilet articles. The diagnosis is made by the examination of smears and cultures taken from the vulva, urethra, vagina and anus. Other forms of pyogenic infection, and also infestation with threadworms, produce symptoms and signs closely resembling those of a gonococcal infection. As gonococcal vulvo-vaginitis may prove unusually resistant to treatment either with penicillin or the sulphonamide drugs, these cases are not suitable for treatment at home, but should invariably be sent into the special hospital accommodation provided by a large local health authority. Penicillin should be given intramuscularly by three-hourly round-the-clock administration. Children tolerate large doses well and a child of 3 years may be given 10,000 units increasing to 15,000, 20,000 and 25,000 units, and treatment should be continued for 6 days, or until about 50 injections have been given. Relapse frequently occurs and is indicated by the return of slight redness of the vulva and the reappearance of gonococci in the smears. These relapses

may sometimes be cured by a course of sulphathiazole or sulphadiazine, in doses of  $\frac{1}{4}$  gram four-hourly with a commencing dose of  $\frac{1}{2}$  gram. Five or six doses are given in the 24 hours, and this régime is maintained (with a good fluid intake) for 5 days. Testing for cure consists in the frequent examination of smears and cultures from all the parts affected, as well as inspection of the vulva for redness and discharge. This bacteriological testing must be persevered with for many weeks or even for months in a relapsing case.

### OPHTHALMIA NEONATORUM

Ophthalmia neonatorum must be notified to the local M.O.H., and for this purpose it is defined as any inflammation in the eyes of an infant occurring within 3 weeks of its birth and accompanied by a discharge. The organisms causing the inflammation may be gonococci but much more commonly are other pyogenic bacteria, such as staphylococci or the bacilli peculiar to conjunctivitis, but no matter what the organismal cause may be, the onus of notification still holds. The diagnosis is established by the demonstration of the causal organisms in smears and cultures of material taken from the surface of the lower conjunctival sac. When the inflammation appears within 48 hours of birth it is more likely to be gonococcal than if it first appears after several days, and, if gonococcal, the infection has been conveyed to the child's eyes during the passage of its head through the mother's genital canal. This means that the mother is also infected, and she must be examined and treated. In such a case, the source of the infection may be the father, and he should also be interviewed, examined and, if necessary, treated. When the inflammation of the infant's eyes arises after several days or more than a week, the infection may still have come from the mother and have been conveyed on her fingers or by a towel, or it may have come from someone else in contact with the child, and the practitioner's responsibility is not liquidated until the problem of who infected the baby has been solved.

The ophthalmia in the baby is usually treated either by parenteral penicillin or by oral sulphathiazole or sulphadiazine, and, when either of these methods is employed, little local treatment of the eye is required beyond washing the pus out of the conjunctival sac with warm sterile saline lotion poured from an undine every  $\frac{1}{2}$  to 2 hours. In addition, drops of 10-20 per cent. sodium sulphacetamide may be instilled four-hourly as this application is non-irritating. As these cases are usually admitted to hospital, a multiple injection technique is easily applied. For a newly born baby the dose of penicillin to be given by intramuscular injection may be 5,000 units to be repeated three-hourly until from 8 to 16 injections have been given. When admission to hospital is impracticable the oral method is more convenient and usually satisfactory. Sulphathiazole or sulphadiazine in doses of  $\frac{1}{4}$  tablet (0.125 gram) is given four-hourly 5 or 6 times in the 24 hours and continued for 5 days. The local application of penicillin in the form of drops of solution of the pure crystalline salt has been advocated, but is not recommended because the solution must be applied so frequently as to demand the services of a special nurse.

The treatment described is effective whether the cause be the gonococcus or not. In all cases where gonorrhoea has been proved to exist, and in most cases where it cannot be ruled out, it is wise to send both mother and baby



into the special hospital accommodation provided. This arrangement means that the mother can continue to breast-feed the baby, and the residence in hospital facilitates not only the full examination of both mother and child but also the investigations directed towards the discovery of the source of the infection, *e.g.*, in the father or in another member of the household.

Prophylaxis at birth is still usually carried out by instilling into each eye two drops of fresh 1 per cent. solution of silver nitrate, leaving this in for 2-3 minutes and then washing it out with warm sterile saline. In the future, drops of solution of "white penicillin" may be substituted for the 1 per cent. silver nitrate.

## SYPHILIS

The situation in regard to the treatment of syphilis may be described as "fluid." When, in December 1943, Mahoney showed that penicillin was effective against *spirochaeta pallida* in vivo, the expectation of being able to treat syphilis with a relatively non-toxic drug became realized. In the past, arsenicals and bismuth had achieved a high proportion of cures in early cases; but these were toxic drugs and their exhibition always involved the risk of provoking undesirable side-effects, some of which, *e.g.*, toxic encephalopathy or exfoliative dermatitis, meant at best a serious and trying illness, and at worst held a real menace to life itself. So penicillin seemed likely to create a new vogue, and was in fact, in June 1944, adopted by the U.S.A. Army Medical Corps in Europe as the ideal routine treatment for early syphilis, the original schedule specifying a total dosage of 2.4 million units in  $7\frac{1}{2}$  days, given as 60 three-hourly injections each of 40,000 units.

A year later came the counterblast of disillusionment in the form of an assessment of the results achieved since the adoption of the 2.4-mega-unit schedule. The review of over a year's experience of the treatment of early syphilis by penicillin alone in what then seemed the adequate dosage of 2.4 mega units gave the results in the form of the percentage failure rates for the different stages, as follows: for seronegative primary cases, 5.28 per cent. failures; for seropositive primary cases, 9.54 per cent. failures; and for secondary cases, 17.4 per cent. failures. As the treatment was carried through to completion in practically every instance, these published results made it clear that penicillin alone, in the dosage named, could not be relied upon to cure every case of early syphilis. The results attained by schedules specifying a lower total dosage were even less satisfactory.

At this stage, when confidence in penicillin was wavering, the experimental work of H. Eagle and others seemed to supply a much needed directive for the guidance of therapists. Eagle, *et al.*, demonstrated that when penicillin and mapharsen (arsenoxide) were used together in the treatment of experimental syphilis in rabbits, the action of these two agents was synergistic: when subcurative doses of mapharsen were combined with it, the amount of penicillin needed to cure the rabbit of syphilis was only a fraction of what was required when the penicillin was used alone. When this discovery was translated into clinical practice by using penicillin and arsenoxide together in combined treatment, it was found that the percentage failure rate was halved when a subcurative dose of penicillin was combined

with a subcurative dose of arsenoxide. Similarly, if bismuth were used along with penicillin, by combining a subcurative dose of penicillin with a subcurative dose of bismuth, the percentage of failure was again almost halved. The natural deduction from this proof of synergism between penicillin and arsenic and between penicillin and bismuth would seem to be that the best treatment for human syphilis is a combination of all three. This plan has the disadvantage of confusing the issue as to the efficacy of penicillin alone, but has the overpowering advantage of holding out to the patient the best prospect of complete cure: it combines the promise of penicillin with the lasting influence of the time-honoured and proved arsenic and bismuth.

### OBJECTIVES IN THE TREATMENT OF EARLY AND OF LATE SYPHILIS CONTRASTED

The lesions of early acquired syphilis, the primary chancre and the secondary moist papules and mucous patches, are infectious, and an important aim of treatment is to prevent spread of the disease by quickly abolishing infectivity. On the other hand, the gummata and gummatous ulcers and infiltrations of late syphilis are not liable to transmit the disease through contagion, so that there is not the same urgent need to start treatment quickly or to make it intensive. Moreover, the spirochaetes in the early lesions are more superficially situated and accessible; whereas in late syphilis the spirochaetes have retired to the viscera and deeper tissues, and into fibrous tissue barriers, where they are much less accessible. Again, the patient with primary or secondary syphilis is commonly a young man or a young woman who is otherwise healthy; whereas the patient with tertiary syphilis may have had his general health undermined by the protracted disease, or, even if apparently healthy, may have sustained cardiovascular or central nervous system injuries which render him liable to be further damaged by any acute reactions from treatment or by the chronic strain of intensive treatment. These considerations indicate that the treatment of early syphilis in the young adult should be intensive and calculated to kill all the spirochaetes and cure the disease as quickly as possible; and that, on the contrary, in late syphilis the treatment should be cautious, because the spirochaetes cannot be killed quickly without running the risk of killing the patient as well, especially if the method of treatment adopted involves the use of toxic drugs. Carrying the argument to its logical conclusion in the practical use of the organic arsenicals and bismuth in the pre-penicillin conventional treatment, the following deductions may be made:—(1) in treating early syphilis the doses of the drugs should be large, and in late syphilis the doses should be small; (2) in early syphilis the most intensive drugs, *i.e.*, the trivalent arsenicals, should be used, and in late syphilis the less intensive drugs, *i.e.*, bismuth and the pentavalent arsenicals, should be preferred; (3) in early syphilis the most intensive route of administration, the intravenous, should be chosen, and in late syphilis the less intensive intramuscular route is safer; (4) in early syphilis the treatment should be concentrated into as short a time as is compatible with safety and efficiency, for then default will be less frequent and less disastrous, and in late syphilis the treatment should be slow and prolonged and continued so long as the patient is deriving benefit.

Even now, after the advent of penicillin as one of our major therapeutic weapons, it is still necessary to state and to emphasize these general principles, because, although it is relatively non-toxic, the exhibition of penicillin itself may be followed by reactions so severe as to be highly undesirable, or even dangerous in susceptible cases, and also because penicillin is so frequently combined with arsenicals and bismuth.

### THE THERAPEUTIC AGENTS

It is intended to economize time and space in descriptions of the various preparations of penicillin, organic arsenic and bismuth, for these reasons:—the appearance, the properties and the peculiarities of the standard drugs are well known, and, in any case, are very fully described in the booklets issued and sent free of charge to any practitioner by the various manufacturing companies. One of these booklets should be acquired and studied by anyone proposing to use the organic arsenicals or bismuth. Further, in every package of these drugs there is a pamphlet giving detailed instructions. Descriptions of the drugs will therefore be limited to what is thought to be necessary to amplify the information so readily available to every user.

### PENICILLIN

Penicillin may be administered either by using aqueous solutions of the sodium salt in a scheme of multiple 3-hourly injections given round the clock, or by employing the suspension of penicillin in oil and beeswax (P.O.B.) to prolong its action and so limit to one the number of doses required in the 24 hours. These methods of using penicillin have already been described in the section on the treatment of gonorrhœa.

As an alternative to 3-hourly injections or to once-daily "P.O.B." it would seem to be practicable, by greatly increasing the individual dose, to cut down the number of injections of aqueous penicillin given in the 24 hours from 8 to 2. It has been shown that when moderate doses are given, penicillin, at the relatively low serum levels attained, is bacteriostatic; but when large doses are employed, *i.e.*, doses of from 100,000 to 500,000 units, then, at the high serum levels induced, penicillin becomes bactericidal. The deduction from this is that it may be found to be adequate to give a massive dose of penicillin, such as 500,000 units (" $\frac{1}{2}$ -mega") twice daily, *i.e.*, night and morning. When giving these massive doses, it is advisable to use the pure crystalline penicillin G ("white penicillin") and the  $\frac{1}{2}$ -mega-unit dose may be dissolved in 2-3 c.c. of sterile distilled water. By the advocates of the ambulatory treatment of early syphilis (*e.g.*, Lloyd Jones, 1945) it is claimed that the maintenance of a consistently high serum content over a period of 24 hours (as by 3-hourly injections) has not been proved to be essential. With regard to the use of "P.O.B." in the treatment of syphilis, Romansky, the originator of the method, claimed that, in his experience, penicillin in arachis oil and beeswax, given once each day, produced as satisfactory results as did aqueous solutions of penicillin given 3-hourly eight times in the 24 hours. On the other hand, while "P.O.B." undoubtedly maintains a bacteriostatic level of penicillin in the serum for longer than the same dose, say 300,000 units, in aqueous solution, never-

theless the 300,000-unit dose in aqueous solution attains in the first two hours a high bactericidal concentration, whereas the same dose in oil-beeswax hardly reaches bactericidal level at all. The significance of these facts, so far as the treatment of syphilis is concerned, cannot yet be estimated. It seems probable also that arachis oil produces a more prolonged action than ethyl oleate, which is sometimes substituted because it is more fluid. Nevertheless, in the case of such a resistant infection as syphilis and as the action of penicillin on *spirochæta pallida* is so much less powerful than its action on the gonococcus, it is desirable wherever practicable to use the 3-hourly round-the-clock injection plan. This of course means that the patient must be taken into a hospital or nursing-home, whereas the once-daily "P.O.B." or the twice-daily  $\frac{1}{2}$ -mega-unit methods allow the patient to remain ambulant, and need not even interfere with his daily work. In the 3-hourly injection schedule the standard individual dose recommended for adults of both sexes is either 50,000 or 100,000 units. The total dose desirable in the different stages of early syphilis may be assessed empirically as follows:—for seronegative primary syphilis, 5 million (5 mega) units; for seropositive primary syphilis, 6 mega units; for early secondary syphilis, 10 mega units; and for late secondary syphilis, 12 mega units.

**Reactions to Penicillin Treatment.**—*The Herxheimer Reaction.*—Owing to the rapid destruction of spirochaetes in the lesions of primary or secondary syphilis, general systemic and focal reactions frequently occur in the first 24 hours of treatment. Such reactions are expressed systemically chiefly as fever and malaise; while the focal reactions include aggravations of the various manifestations, such as swelling at the site of the chancre and of the regional lymph nodes, and an increase, sometimes marked, in the number and brightness of the secondary skin spots. A slight roseolar eruption may become much more profuse, much brighter red and altogether more spectacular. There is no need to stop the penicillin on account of a Herxheimer reaction, unless the symptoms (e.g., laryngitis) are exceptionally severe, as the reaction subsides and passes off spontaneously with continuation of the treatment. The occurrence of a Herxheimer reaction does not depend directly on the size of the initial dose of penicillin: a small dose, of the order of 1,000 units, may cause a sharp rise of temperature to 104° F., while, in another patient, a dose 50 times as great may not produce any constitutional disturbance at all.

*Other Reactions to Penicillin Treatment.*—The injections commonly cause some soreness in the hip muscles: usually this is not severe and passes off quickly when the injections are stopped. Occasionally the site of injection becomes swollen, tense, hard and tender, and it may then be necessary to change to another area such as the outer aspects of the thighs.

Apart from Herxheimer symptoms, the most common general reactions are allergic in character and are expressed as urticaria and generalized pruritus. There may be oedematous swelling of the face, especially the eyelids, or pain in certain joints with restricted mobility. Herpes may occur on the lips or elsewhere, or there may be toxic erythematata. The allergic manifestations, such as urticaria, are improved by injections of  $\frac{1}{4}$ – $\frac{1}{2}$  c.c. of 1/1,000 solution of adrenaline. The new antihistamine drugs (see p. 96) have a dramatic effect in promoting rapid disappearance of the symptoms, which, in any case, tend to subside spontaneously when the penicillin is stopped.

### COMBINED TREATMENT WITH PENICILLIN, ARSENIC AND BISMUTH

In view of the proved synergistic effect of combining penicillin with arsenic and bismuth, it seems desirable in every case of early syphilis to give along with the penicillin one 10-weeks' course of arsenic and bismuth for seronegative primary syphilis; two 10-weeks' courses of arsenic and bismuth for seropositive primary and early secondary syphilis; and three dual therapy courses for late secondary syphilis.

### ARSENICAL AND BISMUTH COURSES FOR EARLY SYPHILIS

The arsenical and bismuth course which is most likely to be well tolerated by the patient, and at the same time to be very efficacious, is one consisting of intravenous arsenoxide (oxophenarsine hydrochloride, mapharside, neohalarsine) given concurrently with intramuscular bismuth. The arsenoxide is given twice weekly for 10 weeks and the bismuth is given once or twice weekly over the same period. The dose of arsenoxide for a man of average weight is 0.06 gram, and for a woman of average weight 0.04 gram given twice weekly. In order to test for any idiosyncrasy, and to establish tolerance, it is advisable to start with a dose of 0.04 gm. for a man and 0.02 gm. for a woman. Each dose should be dissolved in 10 c.c. of fresh, sterile, doubly-distilled and pyrogen-free water: this may be accomplished by injecting 2 c.c. of the distilled water into the ampoule, and, after the drug has dissolved, drawing up first the 2 c.c. of solution and then another 8 c.c. of distilled water into a 10-c.c. syringe. In contrast to the practice observed when giving an intravenous injection of neoarsphenamine ("914"), which should be injected slowly, the intravenous injection of arsenoxide is given quickly, so that the syringe is emptied in less than 30 seconds. In spite of the speed with which the arsenoxide is run into the vein, "speed shock" or immediate vasodilator reactions (such as may happen with "914") do not occur, and the saving of time is a decided advantage when many injections have to be given.

The bismuth may be given in the form of a suspension of the finely divided metal in sterile isotonic glucose solution (injection of bismuth B.P.), 1 c.c. of the suspension carrying 0.2 gram of bismuth. A man of average weight may be given 0.15 gm. twice a week or 0.3 gm. once a week, and for a woman of average weight the doses are 0.1 gm. twice a week or 0.2 gm. once a week.

**Precautions to be taken when giving Arsenical and Bismuth Injections.**—All syringes and needles must be sterilized by boiling immediately before use (see section on Technical Procedures, p. 923). By rigidly adhering to this rule, "syringe-transmitted hepatitis" can be eliminated, and it is now recognized that jaundice occurring in patients receiving antisypilitic treatment was almost invariably syringe-transmitted. The same technique of using only freshly boiled syringes and needles should be adhered to when giving intramuscular injections of penicillin. In a large clinic the glass syringes and needles may be fitted into test-tubes and sterilized in batches in wire cages by pressure steam ( $\frac{1}{2}$  hour at 30 lb. pressure) in an autoclave.

No one should undertake the giving of intravenous injections of arsenical drugs who has not had training and practice in the technique.

Organic arsenic may be given intramuscularly by choosing either the trivalent arsphenamine diglucoside ("stabilarsan") or the pentavalent acetarsol ("acetylarsan"). Both these preparations are in solution and ready for injection. A man may be given 0.3 gm. of stabilarsan intramuscularly twice a week; and for a woman a suitable dose is 0.2 gm. intramuscularly twice a week. Intramuscular stabilarsan causes considerably more pain than does bismuth, and it is therefore better not to exceed 0.45 gm. in a single dose, which may be given once weekly. Acetylarsan may be given intramuscularly to a man in a dose of 3 c.c. twice a week, or to a woman in doses of 2-3 c.c. twice a week. Where there is likely to be any difficulty about giving intravenous injections of an arsenical, the intramuscular route should be preferred, especially in patients who are receiving arsenic and bismuth as supplements to penicillin.

In giving intramuscular injections of arsenicals and bismuth, two needles should always be used, one to extract the dose from the ampoule or bottle and the other to stab into the upper outer quadrant of the patient's buttock. After stabbing the second needle into the buttock, it should be watched for a few seconds to see that no blood appears, indicating that the point of the needle is not in a vein: if blood does appear, the needle should be withdrawn slightly and pushed into another place in the muscle.

**Side-effects of Arsenoxide and Bismuth.**—The toxic reactions of arsenoxide are minimal. Quite often the patient feels a little nausea later in the day, but usually does not vomit, and the nausea passes off quickly so that he is fit for work next day. A slight reduction in the dose may prevent the nausea from occurring, and after toleration has been established by a few reduced doses, it may be possible to return to the full dose. Dermatitis does sometimes occur with arsenoxide, although much less frequently than with neoarsphenamine or with arsphenamine diglucoside, and such dermatitis as does appear with arsenoxide is mild and the severe exfoliating type is rarely encountered.

**Herxheimer Reactions.**—When treatment is begun with arsenoxide, the first dose may be followed in two to four hours by fever and an exacerbation of the symptoms, especially an intensification of a secondary skin rash. This phenomenon usually passes off in about two hours, though its subsidence may sometimes be delayed. The usual interpretation given is that this is a favourable response, and, in primary or secondary syphilis, it is unlikely to be dangerous or to require any modification of treatment. If treatment is begun with penicillin, it is usual to wait until the "Herxheimer" subsides before giving arsenoxide in addition, and under these circumstances there is no recurrence of this type of reaction.

Instead of intravenous arsenoxide, intramuscular arsphenamine diglucoside (stabilarsan) may be combined with penicillin, but any arsphenamine drug may be followed by toxic side-effects, especially dermatitis, which may be exfoliative. Intramuscular arsenic can be given with less risk by using the pentavalent drug, acetarsol (acetylarsan), as already described.

**Other Toxic Reactions to Arsenoxide and Arsphenamine Diglucoside.**—With intravenous arsenoxide or intramuscular arsphenamine diglucoside, vasomotor reactions are most unusual; and, provided all the syringes and needles used are sterilized by boiling immediately before use for every individual patient (as they should be), syringe-transmitted hepatitis will

not result; and arsenical hepatitis with the drugs and doses recommended is a rarity.

Dermatitis is best treated by prevention. A patient receiving an arsphenamine drug should be warned to report to the doctor at once if his skin begins to itch and if a rash appears. If he comes as instructed without delay, the best treatment is to draw off immediately about  $\frac{1}{2}$  pint of blood. When this is carried out in the early stage of erythema, the toxic reaction subsides rapidly as a general rule. The patient should be given a laxative, put on a light diet, and directed to drink in the 24 hours 4-6 pints of water flavoured with fresh orange or lemon juice and sweetened with glucose. The arsenical drug should be discontinued: now that penicillin is available, there is no call to continue with an arsenical after a threatening toxic reaction, and the antisyphilitic treatment should be continued with penicillin, either alone or reinforced only with bismuth. If a dermatitis induced by arsenic should not subside after the withdrawal of blood, the patient should be given intramuscular injections of 2, 3-dimercaptopropanol (B.A.L., *i.e.*, British anti-lewisite). The dose is calculated at 3 mg. per kilo of body-weight, and usually works out at about 2 c.c. of a 10 per cent. solution. According to the severity of the case, the appropriate dose is given 2-4 times on the first day, and once or twice daily thereafter, and the treatment may have to be maintained for 10 days. B.A.L. is effective in about 80 per cent. of cases of arsenical dermatitis, and usually improvement is apparent in 3 days.

*Toxic Reactions due to Bismuth.*—Provided a patient has a healthy mouth, or alternatively has had all his teeth extracted and has been provided with well-fitting dentures, bismuth in the dosage recommended is unlikely to cause trouble. If the patient's oral hygiene has been neglected and he has dirty, decayed, tartar-encrusted teeth and soft, red and unhealthy gums, then bismuth, especially in large doses, may excite an aggravation of the gingivitis. The early symptoms of bismuth irritation in the mouth are a metallic taste, furred tongue, and soft swollen gums which bleed easily and which show a blue line (due to bismuth sulphide) around the necks of the unhealthy teeth, often behind the lower incisors.

Again, as with all toxic effects, the best treatment is prevention, by promoting oral hygiene, and recognizing that there is no need to persevere with a toxic drug when penicillin can be used instead. When the patient has been rendered non-infectious, he may be sent to a dentist for extractions or other appropriate treatment. The bismuth should be stopped altogether if oral hygiene has not been secured; or the dose should be reduced, and the antisyphilitic treatment made to depend upon penicillin.

### THE "FOLLOW-UP" OBSERVATION OF TREATED CASES OF EARLY SYPHILIS

Cases of fully developed or late secondary syphilis treated with penicillin alone will probably still show a positive Wassermann reaction at the end of the penicillin treatment. Success in curing the syphilis will be indicated by a steady weakening of the Wassermann until it reaches negativity, usually in from 2 to 4 months after treatment. A quantitative serological test, Wassermann or Kahn, is helpful, and this should be taken at intervals of one month. After the third or fourth month, a stationary or rising titre of the quantitative S.T.S. (serological tests for syphilis) may be accepted as

an indication that further treatment is necessary, and this further treatment should consist of a combined course of penicillin, arsenoxide, and bismuth as already described. The S.T.S. one month after treatment may be negative, and, if so, they should be repeated at least at 2, 4, 6, 9 and 12 months after treatment. A patient who has received one or more courses of arsenoxide and bismuth concurrently with penicillin should be kept under clinical and serological surveillance for two years, being instructed to report every three months for physical examination and blood testing. The cerebrospinal fluid should be tested at the end of the first six months of surveillance.

### THE INTENSIVE TREATMENT OF EARLY SYPHILIS WITH ARSENOXIDE

In general, it may be said that the longer the treatment lasts the greater will be the proportion of patients who default and fail to complete the course; and that the shorter the time taken to give an adequate dosage the more dangerous does the treatment become, or, in other words, the more the treatment is compressed in time into weeks or days, the higher the fatality rate. The amount of arsenoxide required to cure early syphilis is 1,200-1,800 mg., and if this weight of the drug be administered in so short a time as 5 days by using an intravenous drip, the predicted mortality is about 1 in 200-300. If the total dose be spread out over a period of 20 days by giving by syringe about 60 mg. per day, the mortality to be expected is estimated at about 1 in 400. When all the conditions (*e.g.*, careful selection of patients) are at the most favourable level, a large group may be treated without any fatal casualties, but such an exceptional result is not likely to be maintained when the selection of cases is less strict and if women are included. In peace-time, and with penicillin available, it is doubtful if 20-day intensive arsenotherapy is justifiable: in any case the patient must be in hospital under the supervision of an expert. As the present circumstances render extended use of the 20-day schedule unlikely, a detailed description of this method will be omitted.

Where a shortening of the period of treatment is highly desirable, and if the patient be a man, it will usually be found to be safe to give, concurrently with the penicillin course, daily intravenous injections of arsenoxide for from 5 to 8 days. For a male patient, a dose of 0.04 gm. of arsenoxide, given every day for 5 days along with the penicillin, is very unlikely to cause any serious toxic effect, and with a robust man the daily dose may be increased to 0.06 gm. and the number of days of administration to 8 instead of 5. The reason for choosing the period of 8 days is that, in the 20-day schedule of intensive arsenotherapy, a reaction, which has been variously named "secondary fever" or "toxic erythema of the ninth day," commonly develops between the 8th and 12th days and frequently on the 9th day. In this reaction there is a rise of temperature to 101°-105° F. with malaise, anorexia, headache and injection of the conjunctivæ. The face may be swollen, especially the eyelids, and a rash may appear on the skin. A severe reaction may culminate in exfoliative dermatitis, or encephalopathy, or may result in severe damage to the liver, or such serious blood dyscrasias as agranulocytosis or aplastic anæmia. It has been estimated that this "secondary reaction" may occur in 10-12 per cent. of patients receiving the 20-day intensive schedule, and, as it may develop as early as the 5th day of treatment, its features should be known to any doctor



who undertakes the intensification of arsenoxide therapy by giving daily injections. Toxic encephalopathy is chosen for description as representing a complication which may easily prove fatal.

**Arsenical Encephalopathy.**—This dangerous complication may occur even in the conventional pre-penicillin routine with neoarsphenamine, but is particularly liable to develop in patients treated by intensive arsenotherapy, especially massive arsenotherapy (*e.g.*, treatment compressed into 5 days by using multiple daily injections). It is considered that women are more susceptible than men, and Indians more susceptible than white patients. In women, pregnancy increases the risk of this complication. The mortality from encephalopathy is high, and in Indian patients may reach nearly 70 per cent. The onset may be sudden with convulsions or gradual with either restlessness and apprehension or with drowsiness and confusion merging into stupor and coma. The cerebrospinal fluid very consistently shows a great increase in the protein content which may reach several hundred milligrams per 100 c.c.

Treatment of this complication is difficult, but B.A.L. (see p. 216) has been claimed to be effective in a certain proportion of cases and is worthy of trial. The patient should be nursed propped up in the sitting position. Glucose saline drips and adrenaline may be of value. Like the other severe toxic effects of arsenicals, exfoliative dermatitis, hepatitis, and blood dyscrasias, acute encephalopathy is a good illustration of the old saw that prevention is better than cure, and also constitutes a strong argument for avoiding arsenic altogether in susceptible cases such as pregnant women or Indians and using instead penicillin plus bismuth.

#### THE CONVENTIONAL UNIT-COURSE TREATMENT USING NEOARSPHENAMINE AND BISMUTH

Generally speaking, each unit course comprised 10 weeks of intravenous neoarsphenamine ("914") given once weekly along with intramuscular bismuth given once weekly. The standard weekly dose of "914" for a man of average weight was 0.6 gm. and for a woman 0.45 gm.; while the standard weekly dose of bismuth was 0.3 gm. for a man and 0.2 gm. for a woman. For the first fortnight, until tolerance was established, the weekly dose was given in two half-portions separated by intervals of 2-3 days. By this conventional plan, successive unit courses were given, separated by rest intervals of 3-4 weeks. The number of units required for the cure of early syphilis was variously assessed: allowing a generous margin for safety, it might be estimated that a seronegative primary case would require 4 units, a seropositive primary case 5 units, an early secondary case 5 units, and a late secondary case 6 units.

There was no doubt that if it were carried out regularly and without serious lapses to its due completion, this time-honoured treatment could achieve a high proportion of cures. But the course was long and arduous and demanded a higher standard of morale and stamina than could be reached by many patients. Patients were apt to conclude, and not without some justification, that the "cure" was worse than the disease, and many stopped attending long before the end of the schedule. It has been stated that in the U.S.A. "long-term treatment was carried through satisfactorily in only 25 per cent. of early cases," and, even if defaulters were traced and

induced to return, "in only 50 per cent. was ultimately satisfactory although irregular treatment achieved." Bearing in mind this high defaulter rate, the recent tendency has been to deprecate long-drawn-out schedules: though not discredited, the old-fashioned unit-course plan has been largely discarded in favour of shorter schemes.

### SEMI-INTENSIVE ARSENOTHERAPY

In semi-intensive therapy, the arsenical is given twice or thrice weekly over a limited number of weeks. If neoarsphenamine be used, it has usually been found that intolerance ensues if the drug be given oftener than twice weekly in a dose of 0.45 gm. (for a man) and if the twice-weekly administration be continued for longer than 5 weeks. Such a course has been employed for seamen of the merchant navies, and bismuth was given concurrently in a dose of 0.15 gm. twice weekly. Thereafter a long rest interval of 6 months was allowed followed by a second bi-weekly course, and finally a third course was given, with again a space of 6 months intervening between the second and third courses.

For most schemes of semi-intensive arsenotherapy, however, arsenoxide is the drug chosen because of its lower toxicity, and one method advocated consists in thrice-weekly injections of arsenoxide, preferably with twice-weekly injections of bismuth, over a period from seven to nine or even up to twelve weeks. The average individual dose of arsenoxide is 0.06 gm., and of bismuth 0.2 gm. It has to be emphasized that these schemes are intended to be curative of early syphilis without penicillin, but, with the use of penicillin now definitely established, the interest and practical importance of these schemes has waned and dwindled.

A useful compromise between the prolonged conventional unit-course treatment and intensive arsenotherapy was the American Army plan of 40 arsenoxide and 16 bismuth injections in a period of 26 weeks, in which the arsenoxide was given twice weekly for 10 weeks, then bismuth alone once weekly for 6 weeks, then arsenoxide again twice weekly for another 10 weeks: in addition, bismuth was given once weekly concurrently with the first 5 weeks and also with the last 5 weeks of arsenoxide treatment.

### THE CONDUCT AND CONTROL OF SYPHILIS

**Early Syphilis.**—The diagnosis of early syphilis is made most quickly and surely by finding *spirochæta pallida* in serum extracted from the chancre in primary or early secondary cases or from moist papules, mucous patches, condylomata, or enlarged regional lymph glands in fully developed secondary cases. In late secondary cases it may be difficult to find *spiro. pallida* in the ulcerative skin lesions, and more reliance must then be placed on the serological tests. The existence of early syphilis should always be proved before treatment is begun. It is not justifiable to tell the patient he has acquired syphilis and to start a course of antisyphilitic therapy on presumptive evidence based on clinical appearances only. Only saline lotion should be used to bathe and foment the chancre until microscopical dark-field examination of serum for *spirochæta pallida* has been made, and, if negative, repeated on several successive days. When the diagnosis has been definitely made, eusol lotion diluted with warm water may be substituted

for the saline. There is an urgency about these cases where early syphilis is a possibility, and no delay should be permitted in carrying out all the diagnostic tests, *i.e.*, examinations of serum from lesions and of blood by the serological tests for syphilis (S.T.S.). As soon as the diagnosis has been securely established, and not before, treatment should be started with penicillin (as already described) and reinforced on the second day with arsenoxide and bismuth. When diagnosed, the patient should be told he has got syphilis, and the nature of the disease explained to him tactfully and without either exaggeration or reticence, but emphasizing that his prospect of a complete and lasting cure is very good indeed.

Marriage should be deferred until the scheme of treatment has been completed and the prospective partner should be told the truth. Husbands and wives should be counselled to refrain from sexual intercourse until the chancre has healed soundly and all other signs have disappeared, and at least a month should be allowed for healing to take place. Thereafter marital coitus may be permitted provided the husband wears a condom or the wife a Dutch cap, so that there can be no chance of conception occurring with its concomitant risk of congenital infection of offspring.

**Late Syphilis.**—In contrast to the procedure in early syphilis, the diagnosis in late syphilis is not made by demonstrating *spirochæta pallida* in the exudate from lesions, but now depends on the results of the S.T.S. (serological tests for syphilis) which are considered in relation to the clinical appearances and the history, especially a history of still-births, neonatal deaths and visual and aural defects in the offspring. Once the diagnosis has been made, an essential preliminary to treatment is a careful and comprehensive clinical examination in which special attention is concentrated on the cardiovascular and central nervous systems. When the case comes under notice through the formation of gummata, the likelihood of central nervous system involvement is less than in the absence of lesions of the superficial tissues. When syphilis has been discovered accidentally through the taking of routine S.T.S., the possibility of the existence of an asymptomatic involvement of the central nervous system should not be disregarded, and a preliminary examination of the cerebrospinal fluid may yield information having an important bearing on the nature of the treatment to be given. Another important factor to be taken into consideration in deciding on the most suitable kind of treatment is the frequent association of cardiovascular with neuro-syphilis: aortic incompetence or myocardial degeneration may constitute a contraindication to fever therapy in a patient whose cerebrospinal fluid tests indicate a menacing attack on the parenchyma of the brain.

Gummata and gummatous ulcers of skin, muscles, and soft parts generally, usually heal well and quickly with penicillin or suitable arsenical and bismuth therapy. Gummatous conditions of long bones tend to improve slowly. But in cases of gummatous destruction of membrane-bones, bones of the skull, nose and palate, there is no power of regeneration, and holes in these bones will never close.

In all cases of late syphilis, the question of "cure" must be related to the amount of destruction sustained: it is as impossible to replace a contracted aortic valve cusp or to give back living neurones to a degenerated frontal cerebral cortex or to an atrophied optic nerve, as it is to close a hole in the hard palate or to restore a shrivelled testicle. It is often impos-

sible to hold out to the patient such prospects of improvement as can be done with the disease in the early stages: the inevitable question, "Can I be cured?" must be met with encouragement, but also with discreet reserve. Encouragement can usually include the assurance to the patient and to those attending upon or living with him that he is not infectious: yet, on the other hand, the partner in marriage and the children may have to be examined and blood-tested.

Caution has to be adopted as the guiding principle in the treatment of late syphilis. The too early, too rapid, and too intensive application of a potent remedy like neoarsphenamine or even penicillin may injure the health and endanger the life of the patient by promoting an excessive absorption and disintegration of the disease processes, or by exciting an undue formation of fibrous tissue. This phenomenon has been described by the epithet "therapeutic paradox." For example, in syphilitic aortitis the early use of even moderate doses of "914" may precipitate coronary occlusion: or in cerebral vascular syphilis a single dose of "914" may determine a cerebral thrombosis or hæmorrhage.

In late syphilis, in men especially, glossitis should be looked for, and, if discovered, kept under constant observation. After the initial stage, in which the tongue is swollen, red, smooth and irritable, sclerosis often supervenes, sometimes with superficial leucoplakia, sometimes with the formation of a thick white felt, and ulceration may occur. There is an unfortunate tendency to apply caustics, such as chromic acid, to the ulcers, and the patient himself may continue to irritate the unstable mucosa with excessive smoking or with strong alcoholic liquors. As far as is possible, all sources of irritation should be removed: carious stumps of teeth should be extracted, especially if sharp and rubbing on the edge of the tongue, and oral hygiene secured. Should any suspicion of epitheliomatous degeneration arise, the patient should be referred to a general surgeon and to a radiotherapist without delay.

Gummatous infiltrations are characterized by the formation of fibrous tissue, and these infiltrations may shrink quickly when potassium or sodium iodide is given orally. Whether such rapid shrinkage of tissue is always beneficial and desirable seems open to doubt. Some patients say they feel better during and after iodide treatment: the tolerance of other patients to iodides is so poor that they quickly become miserable with acute coryza and pustular skin eruptions, and in such patients the use of the drug should be abandoned. The usual thrice-daily dose of 15-30 grains (0.9 to 1.8 gm.) of sodium or potassium iodide should be given highly diluted in a tumblerful of water or milk, and 10 grains (0.6 gm.) of bicarbonate of soda and 15 minims (0.9 c.c.) of spirit. ammon. aromat. may be added.

In the congenital form of the disease, manifestations typical of late syphilis may appear in boys or girls or adolescents or young adults of either sex. These young congenital syphilitics usually tolerate treatment with arsenicals and bismuth extremely well, and these older drugs, as well as penicillin, are very effective in clearing up gummatous lesions of such structures as the lips, tongue or tonsil. In congenital syphilis it is unusual to meet with the serious cardiovascular derangements which may give much cause for concern in late acquired syphilis. Moreover, if chronic otitis media be excepted, congenitally infected children may have few of the sources of sepsis which promote intolerance and complicate treatment in

the older patient suffering from late acquired syphilis. For the most part, therefore, in congenital syphilis the employment of arsenicals seldom gives rise to any serious toxic effects, such as blood dyscrasias or exfoliative dermatitis.

In late syphilis in middle-aged or old patients, septic foci in connection with the teeth or nasal sinuses should be looked for carefully. The older men may have chronic cystitis due to prostatic hypertrophy or stricture of the urethra; while the older women may suffer from chronic cervicitis, endometritis or salpingitis. With the general deterioration of advancing age, arsenic and bismuth may not be well tolerated and penicillin may therefore be regarded as the most suitable drug.

### THE TREATMENT OF LATE SYPHILIS

As a combination of penicillin with arsenic and bismuth is accepted as the best treatment for early syphilis, it would seem reasonable to infer that, with the modification of dosage and type of drug made necessary by the very different clinical conditions, the same combination would also be the best treatment for late syphilis.

When there is no evidence of involvement and impairment of the cardiovascular and central nervous systems, and when the disease is apparently latent or showing activity through gummatous formations, the careful preliminary overhaul of the patient should indicate whether or not a Herxheimer aggravation of any lesion is likely to prove troublesome. For example, an increase of swelling at the site of gummatous infiltration of the larynx may cause embarrassment of the breathing; or further swelling within the sheath of an infiltrated optic nerve (and deterioration of vision may be the only symptom) may precipitate transient amblyopia and increase the damage to the nerve fibres with serious loss of vision. A safe introduction to more active treatment may be made by giving sodium or potassium iodide grains 15-30 (0.9 to 1.8 gm.) thrice daily for a fortnight. Alternatively, a beginning might be made with a small (0.1 gm.) dose of bismuth intramuscularly twice weekly for 2-3 weeks. Then, after the preparatory iodides or bismuth, penicillin may usually be started with a dose of 25,000 units three-hourly for 4 injections, then 50,000 units for 4 injections, followed by 100,000 units three-hourly until a total of from 10 to 12 million units has been given. The bismuth may be continued concurrently with the penicillin, using 0.15 gm. twice weekly or 0.2 gm. every 5-7 days until 15 injections have been given. Thereafter, it may be safe to give intravenous arsenoxide 0.04 to 0.06 gm. once or twice weekly or neoarsphenamine 0.3 to 0.45 gm. once weekly for 8 weeks. Naturally, this combined penicillin-arsenic-bismuth treatment is especially suitable for the younger or middle-aged patients, and should not be selected for elderly or debilitated subjects. For the latter penicillin alone should be the choice, and the commencing dose should be reduced to 10,000 or even to 5,000 units for 5-10 injections before increasing to 25,000 and then to 50,000 units. If penicillin alone be administered, the course may be repeated after an interval of three months, and further treatment guided by the clinical response, and perhaps also by the serological improvement, if any. In elderly subjects the objective to be aimed at is always the improvement and maintenance of the patient's health at the highest level, and never the

quick reversal of the serological tests for syphilis. Certainly a decline in titre of the S.T.S. is to be welcomed provided it does not coincide with a decline in the patient's strength and well-being. A patient may be kept feeling and looking remarkably fit in spite of his S.T.S. remaining strongly positive: in fact, blood tests may be of relatively little importance in these cases, and should never be allowed to become, through constant harrowing repetition, an obsession for both patient and doctor alike.

In late syphilis, so long as it is certain that the treatment is doing the patient good, it may be continued by courses separated by rest intervals of several months for four or five years, especially if arsenic and bismuth are the drugs mainly used: penicillin, of course, may materially shorten this period. If the treatment is patently not proving successful, or if it is obviously getting on the patient's nerves, it should be interrupted, though not necessarily abandoned, and the patient observed until such time as a resumption of the treatment seems desirable. "Maintenance courses" of penicillin and/or bismuth once or twice a year should ensure that the patient's condition does not deteriorate.

### SYPHILIS IN PREGNANCY

Although it has only been available for a few years and in general use for a relatively short time, it has already been claimed that penicillin given to pregnant women, used alone and in the small dosage of 1.2 to 2.4 mega units over 7½ days, can prevent congenital syphilis in the child to a degree unattainable by any other therapy. Further, it is effective even if not begun till the pregnancy is well advanced. It remains to be seen whether in the course of time these claims will be fully substantiated and vindicated. The pregnant woman is especially liable to those highly dangerous toxic effects of arsenic, encephalopathy and purpura hæmorrhagica. Nevertheless it is true that expectant mothers for the most part tolerate arsenicals, and even arsenicals and bismuth, astonishingly well, and that in the past these drugs have achieved a great measure of success in lessening the amount of congenital syphilis.

Syphilis in the pregnant woman, just as in the non-pregnant, may be found in any stage—primary, secondary, tertiary, or affecting the cardiovascular or central nervous systems. For primary syphilis there seems justification for using penicillin in the usual amounts (for seronegative cases 5 mega units and for seropositive 6 mega units), either alone or combined with bismuth, if the kidney function is unimpaired, and postponing arsenotherapy till after the confinement. In secondary syphilis, especially advanced secondary cases, the argument in favour of potentiating the penicillin still further by arsenic is stronger, and must be balanced against the possibility of toxic effects and the potential danger to both expectant mother and child. Because of their low toxicity, intramuscular acetylarsan (2.3 c.c. twice weekly) and intravenous arsenoxide (0.04 c.c. twice weekly) are the safest arsenicals: they should not be used for longer than 8-10 weeks without allowing a break of 4 weeks. For secondary syphilis, the dosage of penicillin given during pregnancy need not differ from the dosage given to the non-pregnant woman, *viz.*, 10 million units for early secondary and 12 million units for late secondary cases. To avoid a severe Herxheimer reaction, the commencing individual dose may be 5,000-10,000

units three-hourly for 5 or 10 injections, then 25,000 for 4 injections, then 50,000 for 2 injections, and so to the full dose of 100,000 units until the required total amount has been administered. Instances have appeared in the literature of the use of penicillin being followed by abortion, but with the highly purified penicillin now available, such a sequel is unlikely. It should be remembered that syphilis alone, if acute, is liable to cause death of the foetus, especially between the 4th and 7th month; that the foetus may therefore be dead or moribund at the commencement of treatment; and that an initial severe Herxheimer reaction may result in foetal death. In order to make sure of preventing prenatal infection, some syphilologists advocate giving a syphilitic woman treatment during every successive pregnancy: with a comparatively safe drug like penicillin the argument for this procedure seems to have been strengthened.

### CONGENITAL SYPHILIS

Unquestionably, the best way to "treat" congenital syphilis is to prevent it by detecting syphilis in the pregnant woman and thereafter by administering penicillin to her. By starting treatment in the 3rd or 4th month of the pregnancy, congenital syphilis in the child should be prevented.

The effect upon the foetus of untreated syphilis varies with the age and intensity of the disease. When the foetus does not die in utero, the birth may occur before full time and the premature baby may then present the classical picture—"old man" appearance, sallow withered skin and bullæ on the palms and soles. These premature marasmic babies are difficult to treat and very liable to die suddenly. Penicillin may be given by injection in a dosage not exceeding 20,000 units per kilogram of body-weight in 60 three-hourly injections over  $7\frac{1}{2}$  days, so that the commencing individual dose for a feeble underweight baby might be about 150-200 units.

For infants in whom syphilis has not been recognized early and who are presented for treatment when a few weeks or months old, the dosage of penicillin, according to strength and viability, might be from 20,000 to 40,000 units per kilogram in 60 three-hourly injections over  $7\frac{1}{2}$  days, or 80,000 units per kilogram in 120 injections over 15 days. While those coming in contact with the infant should be warned that discharges from the nose and ears and moist papules in the mouth or on the skin are contagious, they should also know that contagion will be abolished in a day or two after penicillin is started.

On the whole, syphilitic infants tolerate arsenical drugs reasonably well. An effective treatment is to give an intramuscular injection of a very small dose of the infantile preparation of acetylarsan twice a week. Each ampoule of "infantile acetylarsan" contains 2 c.c. of a solution carrying 0.02 gm. of the drug in each c.c., and a suitable bi-weekly commencing dose for feeble underweight babies is one-third of 1 c.c. (=0.0066 gm.). These minute doses may be continued twice weekly for 6-8 weeks, and then gradually increased as the child's weight improves and strength is gained. The arsenical course may be followed by a course of small twice-weekly doses of bismuth. A suitably diluted suspension of bismuth may be prepared by mixing 1 c.c. of the ordinary suspension (1 c.c.=0.2 gm.) with 9 c.c. of sterile isotonic glucose solution in one of the usual rubber-capped bottles: 1 c.c. of this mixture carries 0.02 gm. of bismuth and a

suitable commencing dose for a weakly baby is one-third of 1 c.c. (=0.0066 gm.) twice weekly. As the infant improves and becomes heavier, the dose may be increased gradually to  $\frac{1}{2}$  c.c., and later to 1 c.c., at the same time lengthening the interval between doses to 1 week.

For stronger infants of several weeks or months old, arsphenamine diglucoside (stabilarsan) may be given intramuscularly twice weekly in a dose of 5 mg. per kilogram of body-weight or once weekly in a dose of 10 mg. per kilogram. For a child of 11 lb. the weekly dose of stabilarsan would be 0.05 gm. Both stabilarsan and acetylarsan are in solution ready for immediate use, and are therefore very convenient in practice. When viability has been definitely established, the most effective treatment is a combination of penicillin, arsenic and bismuth. By these means it should be possible to attain clinical cure and reversal of the S.T.S. to negativity. The cerebrospinal fluid should be examined, if possible at the commencement of treatment (*e.g.* in older children), and if the tests show involvement of the central nervous system, treatment should be prolonged and repeated courses of penicillin given in a determined effort to eradicate the disease in early childhood and so to prevent the appearance later on of juvenile paresis or tabes.

In children of school age, interstitial keratitis responds best to a combination of penicillin with arsenic and bismuth. To boys or girls of 12 years, neoarsphenamine may be given intravenously in dosage corresponding to the body-weight, say, 0.15 to 0.3 gm. weekly; and bismuth intramuscularly in doses of 0.1 to 0.15 gm. weekly. It is unusual for congenital syphilitic children of this age to show any of the serious toxic effects of these drugs. As penicillin is virtually non-toxic it may be given concurrently in almost adult dosage, commencing cautiously if a Herxheimer intensification is to be feared, working up to an individual dose of 50,000 units three-hourly, and continuing to a total of 5-10 mega units. Children often do well in the fever cabinet, and a resistant case of interstitial keratitis may be greatly benefited by 2-4 three-hour sessions of electropylrexia. Before the advent of penicillin, these older children were usually treated with successive courses of arsenic and bismuth over a period of 4-5 years according to the response of the S.T.S. With the aid of penicillin it should now be possible to shorten greatly the period of active treatment, but observation should be prolonged, as interstitial keratitis may recur "out of a blue sky" after S.T.S. have become negative. Every endeavour should be made, through the inspections of school medical and dental officers, to detect these congenital syphilitics early in life, through "saddle-nose" or Hutchinsonian teeth, and so to ensure that treatment will be started before the age when interstitial keratitis or labyrinthine deafness usually occur. Prevention of these complications is eminently practicable and successful; whereas arrest of an active process (*e.g.*, nerve deafness) may be exceedingly difficult, and repair of destroyed tissue and restoration of function impossible.

### SYPHILIS OF THE CARDIOVASCULAR SYSTEM

In the cardiovascular complications of syphilis, especially in coronary disease, aortic aneurysm and aortic incompetence, a severe Herxheimer aggravation can be very dangerous. The lives of these patients are precarious; any shock, including "therapeutic shock," may prove fatal. On



the other hand, if their lives can be adjusted to run quietly, smoothly and easily, if worries, excitements, strains and stresses of all kinds can be avoided, and if treatment be applied gently and judiciously, then comparative comfort can often be secured, interest in affairs and a measure of activity preserved, and life kept worthwhile and substantially prolonged.

Syphilitic cardiovascular cases may be further complicated by involvement of the central nervous system, and the therapeutic requirements of these two conditions may not run parallel. For example, decompensated aortic incompetence and myocardial degeneration call for prolonged rest in bed; but if a tabetic, who may also have aortic and cardiac insufficiency, be put to bed for a long period, any existing ataxia may be greatly aggravated. It has already been pointed out that "therapeutic paradox" is another possibility to be guarded against. The wise clinician will not allow the seeming insistence of positive S.T.S. to override his better judgment to the extent of attempting a dangerous intensification of treatment. The rôle of the Wassermann is subservient, and cardiovascular syphilis is a condition in which the S.T.S. may fluctuate irrespective of treatment.

Frequently, therefore, a beginning is made with either iodides or small doses of bismuth twice weekly or both (as already described), until compensation has been improved or regained. So far as is possible, cardiologist and syphilologist should co-operate in the conduct of the case. Signs of improvement are the amelioration of breathlessness, substernal discomfort or anginal pain, tachycardia and œdema of the legs. Soon it should be possible to consider the addition of penicillin, and this should be started cautiously with a small dose of 5,000 units, or less, three-hourly. After the first 24 hours (during which a Herxheimer aggravation would appear), the three-hourly dose may be progressively and gradually increased from 10,000 and 25,000 units to 50,000 or 100,000 units. After reaching a total of 5 mega units, it may be wise to terminate the course, and, later, repeat it after an interval of 3 months. These patients should be quietly supervised throughout their lives, with the doctor in the rôle of guide, philosopher and friend rather than that of an ardent Wassermann hunter. Not much can be said in extenuation of any treatment which eliminates the disease by eliminating the patient. After the advance of the disease process has been checked, the position gained may be stabilized by "maintenance courses" once or twice a year. Usually the damage wrought cannot be repaired, but, if the patient cannot be given a new heart or aorta, at least he can be given new help and a new hope.

### **SYPHILIS OF THE CENTRAL NERVOUS SYSTEM**

According to the stage of the syphilis and the time after onset, the central nervous tissues attacked may be the meninges, or the vessels, or the parenchyma, but commonly all three structures are involved to a greater or less degree. A predominantly meningeal attack may occur comparatively early in the course of the disease, *i.e.*, in the secondary stage; a predominantly vascular attack is a tertiary manifestation and may develop early or late in that stage; while parenchymatous neurosyphilis seldom declares itself sooner than 6-10 years after the onset of the syphilis, whether that be acquired or congenital.

The early meningeal type of attack, due largely to cellular infiltration

rather than to organized fibrosis with replacement and destruction of healthy tissue, is amenable to and controlled by the therapeutic agents normally used for early syphilis, *viz.*, penicillin, arsenic and bismuth. Where the outstanding symptom is headache, with or without some irritability, confusion or other mental change, and the cerebrospinal fluid shows a marked increase of the cellular and protein contents, penicillin should be started cautiously, as a Herxheimer reaction might produce delirium; or else a beginning may be made with bismuth. The later meningeal attacks almost invariably include more or less marked changes in the vessels and the parenchyma and the treatment then is similar to that of vascular and parenchymatous neurosyphilis.

#### VASCULAR NEUROSYPHILIS

While vascular neurosyphilis may declare itself dramatically as a hemiplegia caused by thrombosis of a central branch of one of the middle cerebral arteries, the hemiplegia is frequently preceded by transient seizures in which a part of the brain has its blood supply temporarily cut off. The syphilitic endarteritis has been gradually causing a narrowing of the lumen of the lenticulo-striate branches, and several more or less abortive attacks of hemiparesis or aphasia may give premonitory warnings of the imminence of complete occlusion. So far as treatment is concerned, the situation is quite evidently pregnant with possibilities of disaster. Vigorous treatment, such as intravenous neoarsphenamine with its risk of "therapeutic shock," or a Herxheimer reaction excited by large doses of penicillin, may precipitate a catastrophe fraught with danger to the life of the patient. Rest, with iodides first, and then small (0.1 gm.) doses of bismuth, may pull the patient back from the grave when "914" would push him into it. After 2-4 weeks, according to the severity of the attack, penicillin should be introduced cautiously, starting with a dose of 5,000 units for 10 injections; then 10,000 units for 5 injections, then 25,000 units for 4 injections; and, finally, 50,000 units three-hourly until 10-12 mega units have been given. The 0.1 gm. doses of bismuth should be continued twice weekly for 10-15 weeks. In these cases of cerebral vascular syphilis, the changes in the cerebrospinal fluid may be limited to slight increase of cells and protein, and the Wassermann may be negative. Penicillin treatment usually brings about improvement in the cerebrospinal fluid tests. Repeated and prolonged courses of penicillin may be necessary.

#### TABES DORSALIS

Tabes dorsalis may be a late consequence of acquired syphilis and usually declares itself 10-20 years after the original infection; or it may occur in congenital syphilis and produce recognizable changes from the 10th year onwards. The possible symptoms are numerous and diverse, but the symptom which brings the patient to seek advice may not point obviously to posterior column degeneration in the spinal cord. For example, he may complain of failing vision, or a swollen knee-joint, or abdominal pain and vomiting, or urinary incontinence, or an ulcer on the sole of his foot. Thus, besides the general treatment of the cerebrospinal syphilis, special treatment of the presenting symptom is frequently required.

As always in late syphilis, treatment should be preceded by a careful examination in order to ascertain the extent of the damage sustained, the tissues, systems and functions affected, and the degree of the deterioration. Such an examination will go far towards indicating what lines of general systemic treatment are possible and permissible, and what kind of special treatment will be required. It has already been remarked that syphilis of the central nervous system is frequently accompanied by syphilis of the cardiovascular system: thus, if a tabetic patient has also aortic incompetence, or aortic aneurysm or coronary disease, the question of whether or not he should have fever therapy is answered straight away in the emphatic negative. On the other hand, if a tabetic has such an advanced condition of optic atrophy that he is already blind, the effect of tryparsamide in aggravating optic atrophy is no longer a deterrent to its use, and there need be no hesitation in giving it in full doses; but if the patient has had an atonic bladder and has developed cystitis with urinary sepsis, the existence of this septic focus may lead to intolerance to neoarsphenamine, if an attempt be made to use this form of treatment.

The preliminary clinical examination should include S.T.S. and full tests of the cerebrospinal fluid, *i.e.*, cell count, total protein, globulin, Wassermann, and goldsol. If, in a patient with clinically definite tabes (*e.g.*, Argyll Robertson pupils, absent knee and ankle jerks, and "lightning pains"), all the tests of both the blood and the cerebrospinal fluid are negative, and the disease is therefore in the so-called "burned-out" stage, some authorities assert that penicillin is by this time of no value. On the other hand, if such a patient looks and feels better after a course of penicillin, and says that his lightning pains are less troublesome, should not these criteria be accepted rather than blood or cerebrospinal fluid tests?

The opinions of authorities vary as to the value of penicillin in neurosyphilis. Whether or not it passes the "blood-brain barrier" and appears in effective concentration in the cerebrospinal fluid, there is little doubt that penicillin given intramuscularly can and does produce improvement, both clinical and in the tests of the cerebrospinal fluid. In assessing the probable value of penicillin in any particular case, an attempt should be made to estimate the amount of the damage which is irreparable and the extent to which recovery is possible. For instance, if a knee-joint has been thoroughly disorganized by Charcot's disease, and articular cartilage, bone, synovial membrane and ligaments have been destroyed, it is futile to expect that either penicillin or any other therapy can reconstitute the joint. Penicillin cannot replace dead neurons either in the posterior columns of the cord or in the optic nerves. Moreover, in tabes it is especially difficult to assess the value of any particular treatment because the disease is so liable to undergo spontaneous arrest irrespective of any treatment. These facts should be borne in the mind of the physician when he is discussing with his patient what can and what cannot be expected from the treatment which he is going to apply.

The experience so far available seems to indicate that the two most effective agents at the physician's disposal are penicillin and fever, and that the best results are to be expected from a combination of these two, especially a combination of malaria and penicillin, which may be used simultaneously as penicillin has no effect on the plasmodium. Before the advent of penicillin the treatment given for tabes frequently consisted in successive

courses of tryparsamide or neoarsphenamine along with intramuscular injections of bismuth, either with or without fever as reinforcement. Now that the choice has been extended by the addition of penicillin, the first question to be decided is which of these agents should be used, and whether any of them are contraindicated. Apart from the general contraindications to fever, which will be discussed in the section on paresis, the contraindications inherent in tabes are chiefly the cardiovascular complications. Tryparsamide should not be used if there is advancing optic atrophy. Where there is dental sepsis or kidney insufficiency, bismuth is not a good choice. In the presence of urinary sepsis, or of septic foci in the mouth or elsewhere, neoarsphenamine may give rise to dermatitis or other toxic effects. Apart from the risks consequent upon a Herxheimer reaction (e.g., in aggravating a rapidly progressive optic atrophy or in exacerbating coronary stenosis), the contraindications to penicillin are fewer and limited by its essential non-toxicity.

Wherever it is particularly necessary to avoid a Herxheimer reaction, it is reasonable to start cautiously with penicillin as described in the section on vascular neurosyphilis. Otherwise the commencing dose may be 25,000 units, to be increased to 50,000 units, then 100,000 units three-hourly, maintained until a total of 12 mega units or more has been reached.

Penicillin may be used in conjunction with intravenous tryparsamide and intramuscular bismuth. The tryparsamide is given once weekly in a dose of 3 gm. for a man and 2 gm. for a woman, the usual duration of a course being 10 weeks or longer. Bismuth may be given once or twice weekly in the usual weekly doses of 0.3 gm. for a man and 0.2 gm. for a woman.

The duration of treatment is determined by the clinical response and the response of the S.T.S. and tests of the cerebrospinal fluid. Before the advent of penicillin, treatment was often continued for 4-5 years, but penicillin should serve to shorten the schedule.

**The Treatment of Special Symptoms.**—*Disturbance of Micturition.*—The patient with an atonic bladder should be instructed to pass urine regularly and to see that he empties the bladder completely at each act of micturition. Defective control and difficulty in starting the act of micturition may sometimes be improved by the passing of a full-sized bougie (e.g., Béniqué size 25) into the bladder under strict aseptic precautions. When there is cystitis and urinary sepsis, the infecting organism should be determined by bacteriological examination: if it be sulphonamide-sensitive, sulphadiazine may be given in doses of 1 gm. four or five times daily along with an adequate fluid intake. When the patient has become incontinent, a spell of tidal drainage of the bladder may be very beneficial. As urinary sepsis is a frequent cause of a tabetic patient going rapidly downhill, special attention should be given to this function.

*Lightning Pains.*—These pains may improve under the general treatment, especially under a combination of malaria and penicillin. Temporary relief can usually be obtained by giving a powder containing aspirin 8 grains (0.5 gm.), phenacetin 5 grains (0.3 gm.) and codeine  $\frac{1}{2}$  grain (0.03 gm.) or Tab. Codein. Co., one or two, if necessary, every four hours. The pains may be exacerbated for the time being by malaria therapy or electropyrexia, but the patient may be encouraged by the assurance of improvement when the course of fever is finished.

*Gastric Crises.*—Protracted vomiting will cause dehydration, salt depletion and fall in blood pressure. In these circumstances an intravenous drip of 800 c.c. of 6 per cent. glucose in 0.9 per cent. saline will quickly produce marked improvement. Even under penicillin treatment, gastric crises may prove intractable, and severe and continued pain may justify morphine  $\frac{1}{2}$  grain (0.03 gm.) by hypodermic injection. Malarial treatment is justifiable if the patient be suitable for it (see p. 232).

*Disturbance of Walking.*—The patient with ataxia must be taught by remedial exercises how to control his legs and feet. Until he regains confidence and balance he may walk pushing a wheel chair in front of him, then holding the arm of his wife or a nurse, first with, then without, the aid of a stick. He should practise looking straight in front and not down at the ground. Ataxia tends to get much worse if the patient takes to his bed for a cold or any intercurrent illness, so tabetics should be encouraged to keep out of bed as much as possible. With perseverance and encouragement, great improvement may result.

*Disturbances of Vision.*—A tabetic may have double vision or squint from external ophthalmoplegia due to paralysis affecting especially the muscles innervated by the 3rd and 6th nerves. Paralysis of the branch of the 3rd nerve supplying the levator palpebræ superioris results in ptosis, and this may be partial or complete and is usually unilateral. If the ptosis be complete, the patient cannot see with the affected eye unless he raises the lid with his finger, but if treatment be applied promptly, there is a good prospect of recovery. Failing vision, especially with contraction of the visual fields, may be the symptom which brings the patient to the doctor. In the examination and special treatment of these cases it is always wise to have the co-operation of an ophthalmologist. Early optic atrophy cannot be detected with accuracy merely by looking with an ophthalmoscope for pallor of the optic discs: a perimetric examination of the visual fields is required in addition. Now that penicillin is available, if the ophthalmologist reports commencing optic atrophy with contraction of the fields, it is doubtful if the use of trypanamide is justifiable, as trypanamide is a neurotropic drug and penicillin is not. In cases of advancing optic atrophy, a combination of penicillin with electropyræxia would seem to hold out the best hope of arresting the otherwise almost inevitable progressive deterioration and increasing blindness. In cases where no advance is recorded in successive perimetric field estimations, arrest may occur and the condition remains stationary. If, however, the condition be advancing, so long as adequate central vision remains to him, the patient should be prepared for blindness by being taught Braille and learning a suitable craft. In tabes where the full force of the attack is concentrated on the optic nerves, curiously enough, other systems and functions, including locomotion, are often spared for a considerable time. Apart from his failing vision, the patient's health may be good, but, although his bodily strength is undiminished, his activities are progressively curtailed, and he may have no devoted attendant with sufficient spare time to lead him about and give him exercise. To a sightless man, an Alsatian dog trained to lead him may be a great blessing.

*Trophic Disturbances.*—The cliché that neither penicillin nor fever individually or in combination, nor any other treatment, present or to come, can be expected to achieve the impossible may serve to emphasize that

much of the damage caused by trophic disturbances is irreparable. All the constituent structures of a knee, ankle, hip, foot, lumbar spine, or elbow joint may be destroyed by Charcot's disease, but the process may be fast or slow. An orthopædist should be consulted to help in devising palliative treatment, but appliances designed to take weight and strain off an affected part may put extra strain on other parts and joints and, by doing so, lead to further extension of the arthropathic process. Apart from the help given by palliative appliances, little hope of substantial amelioration can be held out.

A sinus may be associated with a perforating ulcer of the sole leading to the bone above and more or less extensive destruction of the heads of metatarsals and of the phalanges of the toes. A perforating ulcer of the sole can often be caused to close up temporarily by taking the weight off it and keeping it clean, but it is inclined to break down again if these measures be neglected by the patient, as they often are, because the ulcer is relatively painless. Superadded septic infection with inflammation and swelling of the foot improves under the penicillin given for the systemic condition. No treatment can restore the dead bone which so often lies at the top of the sinus leading from the ulcer to the head of the first metatarsal.

*Prognosis.*—With penicillin treatment, reinforced by fever where this is practicable, it may be possible to secure distinct improvement in up to 80 per cent. of cases of tabes. The difficulties in assessing improvement have been emphasized. While apparent arrest may occur, in all cases of tabes there is an inherent tendency towards progressive deterioration: neurons have been destroyed and their place taken by proliferation of connective tissue and by fibrous tissue. This unhealthy environment, accentuated by deficiency of the vascular supply due to endarteritis, must depress the vitality of the living neurons remaining in the area, and may eventually determine a spread of the degenerative process. From this it would appear that the most that can be expected from treatment is alleviation of such symptoms as lightning pains and urinary disabilities, and prolonged arrest of deterioration, which, even in the absence of treatment, may be slow.

#### GENERAL PARESIS

The same considerations which have been elaborated in connection with the treatment of tabes may also in large measure be applied to general paresis: by the time the condition is recognized, ten or more years after the beginning of the disease, organic changes have taken place in the cortex of the frontal lobes of the brain, and while there is no doubt a functional reserve of neurons, there is equally no doubt that to a large extent the organic changes (atrophy of the cortex, thickening and adherence of the meninges, dilatation of the ventricles) cannot be reversed. "Cure" in the sense of recovery of the status quo is therefore impossible, and in embarking on treatment, hope is limited to securing the prolongation of remission, which in any case may occur transiently in the course of the disease.

There is general agreement among syphilologists that the best results are obtained from a combination of fever (malaria or hyperpyrexia) and penicillin. Prior to the introduction of penicillin, those on whom responsibility for the treatment of these cases devolved were inclined to rely chiefly on fever supplemented by the prolonged application of successive courses of intravenous tryparsamide and intramuscular bismuth. Fever, therefore,

takes an important place, and one of the first questions to be decided is whether or not the patient is a suitable case for fever therapy: obviously, it can only be given to early cases in comparatively young subjects who still retain an adequate measure of physical strength and fitness. As with tabetics, so in paresis the selection of suitable treatment depends upon the results of the careful preliminary examination, which should include not only physical observations but also S.T.S. and full tests of the cerebrospinal fluid: these findings serve as criteria on which to base judgments as to improvement.

**Eligibility for Fever Therapy.**—Among those patients who are ineligible for fever are the aged or prematurely senile. If the general physical condition be sufficiently good, age alone should not disqualify, but comparatively few paretics, taboparetics or tabetics are really fit for fever after the age of 55. Success is more likely in patients under 45 years of age. The obese or emaciated and the alcoholics are bad risks, and pregnant women are excluded. Any severe disease or damage of heart, lungs, liver, spleen or kidneys is a contraindication, as is also cerebral vascular degeneration and hemiplegia. The devitalized or anæsthetic skin of paretics, taboparetics and tabetics is easily burned in the inductotherm fever cabinet.

*The Preliminary Investigation* should include X-rays of heart, aorta and lungs and an electrocardiogram; also a complete urine examination especially for albumin and casts and an estimation of the blood urea.

At present, the choice of pyrexial methods is limited by the small number of fever cabinets available and by the dearth of trained nursing personnel. In the circumstances, malaria will probably be the method most widely applicable.

**Malaria Therapy.**—Since its introduction by Wagner von Jauregg in 1887, treatment by induced malaria has been amply justified by many successes. In cases of G.P.I. malaria can achieve improvement, if applied early in the disease, sufficient to put back into commission business or professional men who have shown serious mental changes.

The malaria is induced by inoculating the patient subcutaneously (usually just below the scapula) with 1-10 c.c. (according to the number of parasites per c.c.) of blood taken from another patient in the rigor stage. If not more than 10 c.c. be used, the blood need not be matched, and there is no danger of transmitting syphilis. The rigors usually commence after an incubation period of 10 days or longer, and are sometimes preceded by prodromal fever. During the "chills," the rectal temperature rises to 104°-106° F., remains high for 1-3 hours, and then falls gradually during the next 12 hours. During defervescence the patient sweats profusely. The rigors frequently occur every day and the patient soon experiences malaise, headache, loss of appetite and exhaustion. He therefore requires careful nursing, the more especially as a fall in the blood pressure and anæmia rapidly ensue. If a serious fall in systolic pressure should occur, the malaria should be temporarily interrupted or terminated by the use of quinine (see below). Other conditions demanding temporary interruption or cessation of the malaria are tachycardia with a pulse rate of 120 or over, especially if continued between the rigors; severe anæmia indicated by a fall in the red cell count to 2 million and in the hæmoglobin to 50 per cent.; persistent vomiting; threatened uræmia with non-protein nitrogen above 60 mg. per cent.; or severe jaundice. The malaria may be temporarily

interrupted by an intramuscular injection of 0.2 gm. of sod. bismuth thio-glycollate (thiobismol), or sometimes by giving orally one 2½-grain (0.15 gm.) dose of quinine. When the patient has had 10-14 bouts of fever, the malaria is stopped by giving orally 10 grains (0.6 gm.) of quinine sulphate thrice daily for 5 days, followed by 5 grains (0.3 gm.) thrice daily for another 5 days. Malaria induced artificially is much more easily controlled than the ordinary tropical infection.

It is surmised that one effect of the malaria may be to drive the spirochaetes from the parenchyma of the brain into the meninges, where they are more accessible to antisypilitic drugs, and it has therefore been suggested that, starting 4-5 days after the termination of the malaria, the patient should have a short course of arsenotherapy. Most patients recover quickly when the malaria has been stopped, and will tolerate 8-10 daily intravenous injections of 0.06 gm. of arsenoxide.

With proper selection of cases and adequate nursing care the mortality from malaria should not be more than 2 per cent.

A course of three-hourly penicillin injections, reaching a standard individual dose of 100,000 units, and maintained to a total of 12 mega units or more, should be given either concurrently with, or immediately after, the malaria. With a combination of malaria and penicillin, very definite clinical improvement may be achieved in around 60 per cent. of early cases of general paresis. The question of further treatment is judged by a consideration of all the criteria available, that is, from the clinical observations and from the results of the S.T.S. and the tests of the cerebrospinal fluid. It will take many years before a reliable estimate can be reached as to the efficacy of penicillin in general paresis. In the meantime, all these patients should be kept under regular observation throughout their lives, and, in view of the proclivity of paresis to relapse suddenly after apparent arrest and reversal of the S.T.S. and tests of the cerebrospinal fluid, it would appear reasonable to give one "maintenance" course of penicillin every year.

## CHANCROID

Chancroid is much commoner in tropical countries than in Britain, but may be encountered here, especially in foreign seamen coming into our ports. During this last war, experiences with very large numbers of cases of non-syphilitic ulcers have been recorded. In India, for a period of nine months in 1945, there were nearly 4,000 cases of chancroid among the British venereal disease patients, and over 17,000 cases among the Indian patients: chancroid accounted for 22 per cent. of the British admissions to treatment centres and 31 per cent. of the Indian. Among the Middle East Forces, chancroid was "the commonest form of venereal infection." Naturally, the results of this immense experience will tend to alter some preconceived notions about diagnosis and treatment. In particular, it has been shown that, with proper technique, the diagnosis indicated by the clinical appearances can be confirmed by the demonstration of the causal organism, *H. ducreyi*, in direct smears in nearly 70 per cent. of cases; and also that, by isolating the Ducrey bacillus from other organisms (by planting a small inoculum taken from beneath the edge of the ulcer on to a special culture medium consisting of whole defibrinated rabbit blood), a positive diagnosis by culture can be made in over 75 per cent. of all cases of chancroid. These



reversal of the views previously held that smears were unsatisfactory because of difficulty in interpretation on account of the great numbers of secondary organisms, and that cultures were unreliable because the Ducrey bacillus would not grow in the presence of other bacteria. If positive, smear and culture tests are more satisfactory than a positive Ducrey skin test because this latter is not available until after the lapse of 10 days, and also because positivity may refer to a previous infection. The antigen for the Ducrey skin test (the Ito-Reenstierna test) is an emulsion of *H. ducreyi*: a preparation formerly used, known as Dmelcos vaccine and prepared in Paris, has been off the market and virtually unobtainable for some time. In making the diagnosis, syphilis must always be considered as a possible concomitant as well as an alternative.

In treatment, cleanliness must be secured, because chancroidal ulcers are usually associated with a filthy condition of the skin under a long prepuce. The sub-preputial area should be exposed by retracting the prepuce fully and cleansing the skin surface by frequent washing with, and soaking in, warm saline lotion. In addition to promoting healing, this procedure facilitates finding both the Ducrey bacillus and spirochæta pallida, if these be present also. After a number of successive examinations for spirochæta pallida have been made, a dilute solution of potassium permanganate may be substituted for the saline for bathing and soaking the ulcers, and sulphanilamide may be dusted on them after each soaking. In addition to the local treatment, sulphathiazole or sulphadiazine should be given orally in doses of 1 gm. four times daily after an initial dose of 2-4 gm., and continued for 7-10 days. The patient should be kept in hospital till the ulcers are completely and soundly healed, and should have a "Wassermann follow-up" by the taking of regular S.T.S. for 4-6 months.

In the treatment of penile ulcers, penicillin should on no account be used unless and until a positive diagnosis of syphilis has been made. Fluctuating buboes should be aspirated rather than incised, and aspiration may have to be repeated. If a patient should happen to be sulphonamide-sensitive, the local treatment described above may suffice. An emulsion of the Ducrey bacillus used as a vaccine (Dmelcos) and given intravenously in increasing doses on alternate days may prove a valuable reinforcement of the local treatment: it excites a sharp febrile reaction.

## LYMPHOGRANULOMA INGUINALE

(*Lymphogranuloma Venereum*)

Comparatively few cases of lymphogranuloma inguinale (L.G.I.) are seen in Britain, but it is not uncommon in tropical stations in India, West Africa, Panama, and other tropical countries, and in the Negro population of America. The primary lesion of L.G.I. is a small inconspicuous erosion which heals spontaneously and quickly and in most of the cases is not seen by the physician. Usually, when the patient presents himself, the primary lesion has healed, and the outstanding feature is the adenitis of the inguinal, and sometimes also of the femoral glands, in which already there may be areas of suppuration which may have burst through the skin to form sinuses. L.G.I. may be difficult to distinguish clinically from chancroid, and cases of chancroid in negroes quite frequently give positive tests for L.G.I. The

diagnosis is made either by skin or complement fixation tests, using for the antigen Lygranum S.T. (Squibb) for the skin test and Lygranum C.F. for the complement fixation test. These antigens are prepared by growing the virus causing L.G.I. in the egg yolk sac of the developing chick embryo. For the original skin test as devised by Frei, the antigen used was prepared from pus obtained by aspirating it from an unruptured bubo. This original Frei antigen had poor keeping qualities, and false reactions were possible with it. A patient with L.G.I. may also at the same time have syphilis, or chancroid, or any other venereal infection.

Treatment of the patient seen before fluctuation has appeared in the buboes consists of rest in bed and the administration of sulphathiazole or sulphadiazine in intensive and prolonged dosage, *i.e.*, 4 gm. at once followed by 1 gm. every four hours until a total of 40 or more gm. have been administered. Formerly it was thought that surgical removal of the infected glands, through impeding the lymph drainage, was likely to be followed later by elephantiasis of the scrotum or lower limb. Recently, however, it has been shown that excision of glands which have suppurated, and of discharging sinuses, followed by packing the wounds for 1-2 days with iodoform gauze, combined with the oral sulphonamide treatment, gives good results, shortens the period of disability, and is less likely to be followed by interference with the lymph drainage than would be the case if the sinuses were to persist and cause the formation of fibrous tissue.

In cases where there is a double infection of L.G.I. with primary or secondary syphilis, the penicillin given in treatment for the syphilis may have a beneficial effect on the L.G.I.: the buboes of the latter disease may have subsided by the time the patient has received his quota of penicillin (5-10 mega units) for the early syphilis. On the other hand, it would seem inadvisable to use penicillin for the treatment of L.G.I. with, for example, discharging sinuses (and, therefore, secondary infection), unless the possibility of this procedure delaying the recognition of a concomitant syphilis can be ruled out: an alternative would be to give such a dosage of penicillin as would be curative also for early syphilis.

For the purposes of treatment, the differentiation of L.G.I. from chancroid would not be important, as both respond to sulphonamides, but there may be latent cases of L.G.I., especially in women (who transmit the virus and themselves suffer no disability), and there may be doubt as to whether the virus can survive in the body after apparent clinical cure. As the sequelæ of L.G.I. include chronic ulceration of the genitals (*esthiomene* in the female), and stricture of the rectum, accuracy of diagnosis assumes a further significance.

## GENITAL AND ANAL WARTS

In the past, much confusion has arisen, especially among students, through these warts being misnamed "condylomata acuminata," and also "gonorrhœal warts." The misnomer, "condylomata acuminata," is especially to be deprecated, as it leads to confusion with the "condylomata lata" so characteristic of secondary syphilis. If the word "condyloma" means, as its derivation from the Greek suggests, "a swelling," then these warts, which are excrescences, are inappropriately named. Further, "acuminata" means "sharp-pointed," and a warty mass is often not "sharp-pointed."

Moreover, the soft warts of the genital and anal regions have no necessary association with either syphilis or gonorrhœa, although either, or both, of these conditions may coexist. These questions of nomenclature have an influence on judgment as to suitable treatment: the writer has known anti-syphilitic treatment to be insisted upon in a case of warts (dubbed loosely "condylomata") at the anus in a pregnant woman; and the erroneous description "gonorrhœal warts" may lead a married man to think he is suffering from gonorrhœa with all its implications.

These warts are caused by a virus infection and may be transmitted by contacts, either heterosexual or homosexual: if the latter, obviously treatment demands something more than the mere removal of the consequences, although any attempt to treat the perversion is likely to be fraught with difficulties of the most formidable kind.

A suitable treatment for some (but not all) cases of warts is the local application of a 25 per cent. suspension of podophyllin in liquid paraffin. This treatment must be very carefully done, and is usually most satisfactory if the patient be taken into hospital. If he be allowed to apply it himself, there is a considerable likelihood that the patient will overdo it and allow the fluid to seep over on to surrounding unprotected skin: this results in painful and sometimes extensive excoriations with inflammation and swelling. In making the application properly, the area containing the warts should first be thoroughly washed with soap and water and then dried. Next, the unaffected skin is protected by smearing it with vaseline. Then the podophyllin-paraffin is applied carefully to the warts, working it into all the interstices by means of an "orange-stick" (familiar in manicure). Thereafter the area may be covered with a thin layer of gauze. The podophyllin suspension is allowed to act for 6-8 hours, and then washed off with soap and water. The action of the podophyllin is delayed, and should be observed for 2-3 days. In successful cases the warts become bluish-grey and then disintegrate. Several applications may be required, and, in the intervals between them, the part should be washed with soap and water twice daily and dusted with a dusting powder containing 10 grains (0.6 gm.) of zinc oxide, 20 grains (1.2 gm.) each of bismuth subgallate and light magnesium carbonate in each ounce, the vehicle being powdered starch.

If the patient has a long prepuce, and the warts involve its inner surface and orifice as well as the glans penis, many of the warts will be removed and the cleanliness of the part improved by circumcision. The remaining warts may be removed with the electric cautery (used at a very dull semi-red heat) under general or local anæsthesia. This is the most generally applicable treatment, and usually very satisfactory, and the sloughing bases of the warts do not cause much pain. Thereafter the part must be kept clean with soap and water and dry with the dusting powder, as warts are liable to recur. •

## BALANITIS AND BALANO-POSTHITIS

If the patient has a tight prepuce, balano-posthitis (inflammation of glans penis and inner surface of prepuce) may readily occur in association with gonorrhœa, chancre, chancroid, warts, or with any combination of these. A primary syphilis may masquerade as a balanitis. Phimosis and chronic balano-posthitis in an older man may conceal and disguise the

commencement of an epithelioma. In the younger man, if phimosis be the cause, either circumcision or enlargement of the preputial orifice is indicated. If the prepuce be retractable, the inflammation and superficial excoriation will usually clear up quickly by frequent bathing with and soaking in warm saline, followed by introducing a thin layer of wool, moistened with saline, between the skin surfaces. The saline does not interfere with diagnostic tests, and, after the search for *spirochaeta pallida* or the Ducrey bacillus has been abandoned, then a dilute solution of potassium permanganate may be used instead of the saline, or, as an alternative, eusol diluted 1 part to 2 of warm water.

If the prepuce be not retractable and circumcision is to be undertaken, the operation should be postponed until the acute inflammation and purulent discharge have been subdued by frequent (2-4 hourly) irrigation of the sub-preputial sac with warm saline introduced through a fine cannula passed into the sac through the small preputial orifice.

Recently, treatment by the local application of a solution of penicillin has been advocated for these cases of balanitis in which dark-ground examination of the sub-preputial discharge reveals numerous spirochaetes of types other than *spirochaeta pallida* (e.g., *refringens* and *gracilis*). The method consists in the introduction into the sub-preputial sac of 1 c.c. of penicillin solution carrying 20,000 units. By pulling forward the prepuce and holding the penis up, the solution is kept in contact with the inflamed and excoriated skin surfaces for 15 minutes and then allowed to run out. The procedure is carried out once only and it is claimed that it does not cause healing of a chancre, thereby disguising syphilis, and that *spirochaeta pallida* reappear in serum from a chancre in 2-3 days. Any case of balanitis so treated, however, should be observed and have blood taken for S.T.S. over a period of 4 months.

## NON-GONOCOCCAL URETHRITIS

### (Non-specific Urethritis)

Apart from traumatic causes, many organisms other than the gonococcus may cause a urethritis. Included among the infections resulting in urethritis are those due to staphylococci, streptococci, diphtheroid bacilli, *B. coli*, *B. proteus*, and the *trichomonas vaginalis*. To determine the cause, all the usual diagnostic tests should be applied, including smears, cultures and S.T.S. A thin serous discharge may be due to an intrameatal chancre which may be suspected by the induration it produces and proved by demonstrating *spirochaeta pallida* in "dark-ground" examination.

The treatment selected depends upon the cause as revealed by the diagnostic tests. A slight residual urethritis persisting after the treatment of gonorrhoea by penicillin or sulphonamides will often disappear after a few urethral irrigations with 1 in 10,000 solution of potassium permanganate or 1 in 5,000 solution of chloramine-T.

If, from the onset, the organisms causing a urethritis are sulphonamide-sensitive or penicillin-sensitive, the appropriate treatment should be effective, though often daily or twice-daily urethral irrigation for a few days produces rapid resolution.

A *B. coli* infection is often secondary to a stricture of the urethra or a calculus somewhere in the urinary tract, and to clear up the condition the

stricture must be dilated or the calculus removed. The further treatment is dealt with in the section on urinary tract infections (see p. 788).

**Reiter's Disease.**—A non-gonococcal urethritis is a prominent feature of the syndrome which has come to be known as "Reiter's disease." Besides a urethritis, this syndrome includes polyarthritides and inflammation of various tissues of the eye, *e.g.*, conjunctivitis, iritis and episcleritis. It has been suggested that this combination of symptoms may be due to the pathogenic activities either of a virus or viruses, or, alternatively, of pleuropneumonia-like organisms, but in neither case has the etiological relationship been established conclusively. No bacteria are found in the usual smears and cultures of the discharge. The symptoms of Reiter's syndrome are not relieved either by sulphonamides or by penicillin. Probably artificial fever, induced by intravenous T.A.B. vaccine or by inductothermy (inductotherm fever cabinet) or by hyperthermy in the Kettering cabinet, is the best form of treatment. In these cases of Reiter's syndrome there is often an associated skin eruption on the glans penis and this clears up well under inductopyrexia. The joint swelling is inclined to be resistant and may recur after initial improvement. The urethritis usually responds well to electropyrrexia. Probably the condition is self-limited, but, if untreated, the course may be prolonged.

"Abacterial pyuria" is the descriptive name which has been given to a form of urethritis and cystitis in which none of the usual infective agents can be demonstrated, but which responds well to 3 or 4 intravenous injections of N.A.B., in doses of 0.3 gm. to 0.45 gm., given at intervals of 3-7 days. Here again penicillin and the sulphonamides are ineffective. The cause of "abacterial pyuria" has not been conclusively elucidated: because of the response to trivalent organic arsenical a spirochæte has been suggested as the etiological agent.

Tuberculous infection of the genito-urinary tract is not a common cause of urethritis but should be excluded.

R. C. L. BATCHELOR.

# COMMON TROPICAL DISEASES

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## INTRODUCTION

THE selection of the tropical diseases, the treatment of which is discussed in this section, was made to meet the requirements of students and practitioners in this country, for whom this book is primarily intended. In the course of their practice they may meet with examples of the diseases listed from time to time; further, as modern methods of communication with tropical countries increase in frequency and speed, they may expect in the near future to meet with such diseases more frequently than at present. The omission of other tropical diseases has been made not because they are unimportant but because they will not be met with at all in this country—or extremely rarely. For those who propose to devote themselves to a career in the tropics, a specialized training is essential. Some diseases that are usually included in textbooks of tropical diseases will be considered in other sections of this book, *e.g.*, deficiency diseases, beri-beri, pellagra, scurvy; bacillary dysentery; certain parasitic skin diseases; climatic bubo, etc.

In all diseases an accurate diagnosis is an essential preliminary to treatment. In the case of tropical diseases it is specially important because a number of specific drugs are available, which, if administered early, give very striking therapeutic results.

The practitioner will be asked by patients, proposing to go to the tropics, what steps they should take to prevent infection. To help him to answer this important question, a short account of personal prophylaxis is given under the diseases discussed. In this connection special attention is drawn to p. 217, which details information regarding recent discoveries (including D.D.T.) in vector control, with which all those proceeding to the tropics should be familiar. It will be noted that, among other measures, some specific drugs employed in the treatment of the disease can also be used prophylactically to prevent attacks.

Perhaps it might appear that too many preparations of specific drugs have been mentioned, which might rather confuse the practitioner. However, it has been found that the same infection, *e.g.*, leishmaniasis, malaria, trypanosomiasis, etc., in different parts of the tropics may respond differently to the same preparation, necessitating the trial of other preparations. This is the reason for listing a number of drugs.

Before the war a section on tropical diseases might perhaps have been of more or less academic interest to practitioners in this country, but war service has brought many into a closer and more practical relationship with them; and as an aftermath of war there is hardly a practitioner in the country who will not encounter cases of tropical disease at some time or another. The possibility of obscure symptoms being due to tropical disease should be kept in mind, as these disorders not infrequently

present symptoms which are by no means classical and may readily be overlooked.

## MALARIA

**Specific Therapy.—Drugs Employed.**—Quinine, an alkaloid derived from the bark of different species of cinchona. The constituents of cinchona bark are certain acids, tannin and cinchona red with the following alkaloids: cinchonine, cinchonidine, cuprein, cinchonamine, quinamine, quinine, quini-dine, hydroquinine. A cheap and largely used preparation is cinchona febrifuge, which contains all the alkaloids in the bark. It has the disadvantage, however, that the alkaloid content is liable to vary in different samples. Accordingly, a standard preparation called totaquina has been produced containing 70 per cent. of crystalline alkaloids, of which not less than 15 per cent. must be quinine. Three synthetic preparations are mepacrine hydrochloride (B.P.), pamaquin (B.P.) and the recently introduced paludrine (I.C.I.).

**Treatment of an Acute Primary Attack of Malaria.**—It has been suggested that it might be advantageous, in order to allow of the development of immunity, to permit the patient to have several rigors before arresting the infection. This might be permissible and perhaps advisable in an infection with the benign forms, but it would be too dangerous in the severe malignant tertian malaria.

In an ordinary case without complications, a useful scheme of treatment for an adult is to give 3 gr. (0.18 gm.) of calomel at night, followed by a saline purge in the morning. Quinine is then given by the mouth in the following prescription:—

R	Quinin. Sulph.	.	.	.	.	gr. x (0.6 gm.)
	Pulv. Acid. Cit.	.	.	.	.	gr. xx (1.2 gm.)
	Mag. Sulph.	.	.	.	.	gr. x (0.6 gm.)
	Sp. Anis.	.	.	.	.	℥iii (0.17 c.c.)
	Syr.	.	.	.	.	fl. dr. i (3.6 c.c.)
	Aq.	.	.	.	ad	fl. oz. i (28.4 c.c.)

Sig.—One oz. (28.4 c.c.), t.i.d., two and a half hours after food for one week. Dose then reduced to  $\frac{1}{2}$  oz. (14.2 c.c.), b.i.d., for further two weeks. Totaquina, which contains all the alkaloids, may replace the quinine in the above prescription.

On the completion of the course of quinine, pamaquin (one tablet, containing 0.01 gm.) may be given twice daily after food for ten days. Children require smaller doses of quinine than adults, and the taste has to be disguised. One-twentieth of the adult dose is given for each year up to fifteen years; above this the adult dose is given. A useful method of administration to children is to make an emulsion of quinine sulphate in olive oil, or liquid paraffin containing 32 gr. (2 gm.) to the ounce (28.4 c.c.). This should be well stirred and the required amount floated on a little cold, sweetened milk followed by a further drink of milk. Tablets of quinine made by good firms are satisfactory, but solutions are preferable.

In cases where administration of quinine by the mouth is contra-indicated—*e.g.*, severe vomiting—the drug may be given intramuscularly. For this purpose the best salt is 10 gr. (0.6 gm.) of quinine bihydrochloride dissolved in sterile saline and put up in 2 c.c. ampoules ready for use. The best site for injection is the gluteus maximus muscle at a point on a line horizontal with the tip of the great trochanter. It is very important to avoid the neighbourhood of the large nerves, otherwise serious damage may be done. The injection may be repeated on three consecutive days. For children, proportionately smaller doses are given. The injections should be made very slowly. Mepacrine methanesulphonate in a dose of 0.3 gm. can be given instead of quinine, and has been found very useful.

In severe cases of malignant tertian malaria, where a rapid and powerful action is required, quinine may be given intravenously. The salt employed is again 10 gr. (0.6 gm.) of quinine bihydrochloride in 20 c.c. of sterile distilled water. The injection is made into the median basilic vein at the front of the bend of the elbow. It should be made *very* slowly, at least five minutes being spent over the injection. If given too quickly there may be a rapid and alarming drop in blood pressure. One dose is usually sufficient to control the symptoms, though it may have to be repeated in very severe cases. Thereafter the drug should be administered by mouth. For children, the dose is again adjusted according to age.

In some cases there is an apparent failure of quinine to check the infection. This may be due to a wrong diagnosis or, on the other hand, the patient may not be taking the quinine prescribed. To settle the latter question, a convenient test is available. Quinine is excreted in the urine, and a reagent, Mayer-Tanret, can be used for its detection. The reagent is made up as follows:—

Hydrarg. perchlor.	.	.	.	.	gm. 1.3
Aq.	.	.	.	.	75 c.c.
Mix with					
Pot. iod.	.	.	.	.	gm. 5
Aq.	.	.	.	.	20 c.c.

in a 100 c.c. flask.

Add a few drops of this reagent to the urine, and if quinine is present a white deposit occurs. If albumin is present, heat and filter whilst warm, then apply test. It is important to make certain that the patient is taking no other alkaloid than quinine. If this is done, the test is very reliable and useful, though not absolutely infallible, as very occasionally a patient who is actually taking quinine will show a negative reaction. The cause of such negative reactions is not yet clear, but may be due to an excessive destruction of quinine by the tissues of the individual.

The introduction of mepacrine, pamaquin and particularly palufrine has improved the prophylactic and curative treatment of malaria considerably. These drugs are not derivatives of quinine but synthetic products, manufactured with comparative ease. Mepacrine and pamaquin are the British pharmacopœial equivalents of atebirin and plasmoquine respectively, which were originally German preparations. Mepacrine, like quinine, is a schizontocidal agent acting mainly on the asexual stage of the malaria parasite; it is this stage which causes the clinical symptoms; it has less action on the sexual stage. Pamaquin, on the other hand, is chiefly a gametocytocidal agent and



acts on the sexual stage, especially that of the malignant tertian parasite. Hence the most effective treatment of malaria is a combination of quinine or mepacrine and pamaquin. Mepacrine is dispensed in bottles of  $25 \times 0.10$  gm. tablets. For adults and children over twelve years the "loading" dose for the first day is up to 1.0 gm. and then three tablets daily, each tablet containing 0.1 gm., ground up and administered in a little water or milk during meals. To prevent symptoms of intolerance, large quantities of fluid should be taken. The dose for children from six to twelve years is two tablets daily; from three to six years one and a half tablets; from one to three years one tablet; under one year half a tablet. Mepacrine should be given daily for from six to eight days, the total dose for an adult being 2.5 gm. Quinine hydrochloride in doses of 5 gr. (0.3 gm.) twice a day given along with mepacrine produces a better result than either drug alone, particularly in the case of subtertian malaria. Mepacrine is not contraindicated in pregnancy, cardiac disease or blackwater fever. In severe cases where a rapid action is required mepacrine methanesulphonate is given. It may be obtained in ampoules containing 0.10 or 0.30 gm. of the drug. The content of the ampoule is dissolved in 1.5 to 5 c.c. sterile distilled water, and is given by intramuscular or subcutaneous injection in a daily dosage the same as that of the ordinary mepacrine. Parenteral treatment is indicated in cases of coma, in very young children and where vomiting is present.

Pamaquin is dispensed in containers of  $25 \times 0.01$  gm. tablets and in ampoules of 1 c.c. (1 per cent. solution). The course of mepacrine is followed after a rest of two days by a five- to ten-day course of one tablet of pamaquin twice or thrice daily for adults, with appropriately smaller doses for children. Pamaquin is a highly active substance and the prescribed dosage must not be exceeded. The drug should be used with caution in cases of hepatic dysfunction and of severe anæmia.

Paludrine (I.C.I.) is superior to all known anti-malarial drugs. It is a powerful schizonticide and acts by adversely affecting nuclear (chromatin) division, possibly by depriving the organism of a factor taking part in some essential enzyme reaction. Its action is identical in malignant and benign tertian malaria. It is not gametocidal, yet sterilization of the infection takes place in the gut of the mosquito vector fed on *falciparum* (M.T.) or *vivax* (B.T.) gametocyte carriers as early as one to two hours after the first dose of the drug is taken. M.T. infections are radically cured by a course of 300 mg. (one 100-mg. tablet thrice daily) for ten days. In B.T. infection this course should be followed by one tablet twice weekly for six months to prevent relapse.

*Treatment of Relapses in Malaria.*—Paludrine being a complete causal prophylactic for M.T. infection, the course detailed above will certainly prevent relapses. For B.T. infection one tablet twice weekly for six months as noted above is required. Pamaquin prevents relapses of B.T. infection and may be given with paludrine or quinine. Thus a course of 300 mg. of paludrine and 30 mg. of pamaquin daily for ten to fourteen days will be valuable.

*Toxic Effects of the Specific Drugs.*—Quinine as a rule only causes slight tinnitus, but in some persons with an idiosyncrasy to the drug other symptoms may develop. These are: urticaria, hæmorrhages, bradycardia, gastric disturbance and amblyopia (which has to be distinguished from malarial amblyopia). Even death from syncope may occur. Mepacrine

is of low toxicity, but in susceptible individuals, particularly towards the end of the course, the drug may give rise to gastric discomfort, occasional headaches, toxic psychoses, blurring of vision and lichenoid skin lesions. There appears also to be some tendency to cumulative effect, and care should therefore be taken to ensure proper spacing of doses and courses of treatment. Being a dye its administration may be followed by a harmless yellow pigmentation of the skin, which may sometimes tint the conjunctivæ and give rise to confusion with jaundice. Pamaquin is a highly active substance and toxic symptoms may appear if excessive dosage is given, *e.g.*, severe epigastric pains, nausea, vomiting, headache, cyanosis and methæmoglobinuria. Paludrine has a very low toxicity.

**Malaria in Pregnancy.**—Mepacrine is well tolerated even in comparatively large doses by pregnant women, and is indicated when pregnancy is present in preference to quinine.

**Non-specific Therapy.**—In severe cases of cerebral malaria, after intravenous injection of quinine, lumbar puncture may be performed and 20 c.c. of cerebrospinal fluid withdrawn. This may greatly relieve the cerebral symptoms. If vomiting is persistent, 10 minims (0.58 c.c.) adrenaline, 1 : 1,000 may be given by the mouth in a little water. This has given good results in practice. For hyperpyrexia, cold packs or baths are essential if the temperature is over 106° F. (41° C.). The rectal temperature should be taken, and when it falls to 102° F. (39° C.) the patient should be removed from the cold pack, or bath, and warm blankets applied. In malarial cachexia with marked splenomegaly, counter-irritants (ung. hydrarg. biniodide) should be rubbed in over the splenic area. The Ascoli treatment has been found useful in the treatment of splenomegaly in malaria. It consists of the intravenous injection of  $\frac{1}{100}$ ,  $\frac{1}{50}$  and  $\frac{1}{25}$  mg. of adrenaline in increasing doses up to  $\frac{1}{10}$  mg. Usually about twenty injections are necessary. The contraction of the spleen produced by adrenaline causes the parasites to be ejected from the spleen into the peripheral circulation, thereby rendering them much more susceptible to treatment by quinine subsequently administered. Further experience with this method of treatment in Kenya has confirmed the favourable opinions formed of it. In these cases a course of quinine and acetarsol (*e.g.*, quiniostovarsol, May & Baker) may be given subsequent to the above treatment, two to four tablets morning and evening with meals for ten days. If anæmia is very severe (*i.e.*, below 30 per cent. Hb.) and the patient very collapsed, a blood transfusion should be given. In the majority of cases full doses of iron in the form of ferrous salts will rapidly restore the blood to normal. Helminthic infections are frequently present in malaria and should be treated on lines that will be discussed later under this heading. The disinfection of the patient greatly assists the specific therapy (quinine and synthetic drugs).

**General Management.**—Every case of malaria with fever should be treated seriously and carefully nursed in bed, as severe symptoms may develop without warning in the malignant form. The patient should be given plenty of water and lemonade to drink, as he may be very dehydrated by the profuse sweating. The addition of glucose to the lemonade is useful, since in many cases of malaria a toxic hepatitis occurs. Food at first should be fluid and easily digested. In convalescence, if the appetite is good, a full diet may be given.

### BLACKWATER FEVER

This is a very serious and urgent complication of malaria, most frequently of the malignant tertian infection. The first essential in the treatment is to put the patient at once at complete rest, no matter how unsatisfactory his surroundings may be. Transportation is very badly tolerated.

Suppression of urine is the most serious complication. Recent methods of treatment are based on the view that it is due to a renal anoxia and similar to that which occurs in the "crush syndrome." The principles of treatment are: (1) *Replacement of fluid and salt*. The intake of fluid should be roughly balanced against output. It is a mistake to push fluid too vigorously and it is best given by mouth, but if there is much vomiting normal saline may be given by intravenous drip transfusion. (2) *Blood transfusion*. If the red cell count falls to 1.5 million per c.mm. transfusion is necessary, either with citrated blood or a concentrated red cell suspension in saline. It is essential to cross-match the donor's corpuscles with the patient's. (3) *Alkalis*. Twenty to thirty gm. in the twenty-four hours of sodium citrate or bicarbonate should be given. Large doses may be dangerous. They are best administered by mouth, but if this is contraindicated then sodium bicarbonate, 150 gr. (9.0 gm.) in a pint of saline, may be given intravenously. If the anuria persists in spite of treatment, heat applied to the kidney by hot colonic irrigation may be tried. Recently high spinal analgesia has been used with success to relieve the cortical renal ischaemia. Morphia should be given, especially if there is restlessness or vomiting. Good nursing is extremely important, but in certain cases this may not be available in the tropics. As a rule, parasites are very scanty in the blood. If present, a course of mepacrine as outlined above may be administered. Quinine itself should not be used.

### PERSONAL PROPHYLAXIS OF MALARIA AND BLACKWATER FEVER

**Chemoprophylaxis.**—Paludrine and to a lesser extent pamaquin and prosectasine are *causal* prophylactics of malaria, having a lethal action on the exoerythrocytic forms (E.E.), cryptozoites and metacryptozoites, found in tissue cells and formed from the sporozoites injected by the mosquito. Recent important work has proved that in the E.E. stage of mammalian malaria, *P. cynomolgi* is passed in hepatic parenchymatous cells. *P. cynomolgi* closely resembles the *P. vivax* of human malaria. This property is not possessed by mepacrine or quinine. Paludrine has a completely lethal action on the E.E. forms of *P. falciparum*, but partially lethal on those of *P. vivax*. Clinical attacks of the latter will not occur if the maintenance course given above is adhered to. One tablet (100 mg.) twice weekly at three- to four-day intervals gives complete protection in malarious areas against *P. falciparum* infections, and will effectively suppress *P. vivax* infections throughout the period of drug administration.

Mepacrine is the best drug for the *suppressive* treatment of malaria and superior to quinine. The course, which must be rigidly adhered to, is one tablet of mepacrine (0.1 gm.) daily for twenty-one days before entering, during the entire period of stay in, and for four weeks after leaving, the malarial area. Such a course will suppress and radically cure malignant malaria with all its serious complications, such as blackwater fever, but

relapses of benign malaria will take place and will have to be treated as they occur. It not only acts as an indirect gametocytocidal agent against malignant tertian crescents, but also as a direct one against the gametocytes of benign tertian and quartan malaria. In addition it reduces the number of acute attacks which are followed by showers of gametocytes into the peripheral blood. With suppressive treatment by mepacrine, gametocyte carriers should be effectively controlled. Mepacrine was employed on a vast scale during the war and toxic symptoms were slight.

Paludrine will probably replace mepacrine in the future for a variety of reasons: only a small dose is required; it is non-toxic; it does not discolour the skin; one 100-mg. tablet twice weekly is a complete prophylactic for M.T. and a partial prophylactic and complete suppressive for B.T. infections; it controls the mepacrine-resistant strain of *P. falciparum*.

**Protection against Bites of Mosquitoes.**—The best personal prophylactic is a good mosquito curtain on the bed. It must be free from holes and in good condition. It should be well tucked under the mattress before sunset. It is advisable, as a precaution, when the person has got into the net to examine the interior carefully with an electric torch to see that there are no mosquitoes enclosed. The use of insecticides (including D.D.T.) and repellents is described in detail on p. 277. The dwelling-house should, if possible, have the doors and windows screened, and should not be built in the neighbourhood of native quarters. Persons who have had severe attacks of blackwater fever should, if circumstances permit, avoid returning to the tropics.

## AFRICAN TRYPANOSOMIASIS

**Specific Therapy.**—*Drugs Employed.*—Bayer 205 (Germanin); British equivalent, Suramin (B.P.); French equivalent, Fourneau 309. Tryparsamide; French equivalent, Fourneau 270. Stilbamidine, equivalent, 4:4; Diamidino stilbene; Pentamidine, equivalent (M. & B. 800), 4:4; Diamidino diphenoxy pentane; Propamidine, equivalent, 4:4; Diamidino diphenoxy propane; Pentamidine isethionate (M. & B.).

*Treatment of an Early Acute Infection.*—In the early stages treatment with suramin may be sufficient. It is given intravenously, 1 gm. being dissolved in 10 c.c. sterile double-distilled water and injected slowly into a vein at the bend of the elbow. This is repeated until a total of 5 gm. have been given. If this quantity is given within a week, a maximum effect is produced on the organisms. In some parts of the tropics a single dose of 1 gm. of suramin is administered and followed by tryparsamide, 9 doses of 2 gm. at 5-day intervals.

The aromatic diamidines have been found useful in early cases, and, in such cases, cause rapid sterilization of the blood. Pentamidine has been found more effective and less toxic than stilbamidine. It is given intravenously in doses of 100 mg., dissolved in 10 c.c. of sterile double-distilled water. This dose is given daily for twelve days, children under ten years receiving half the dose. The administration of the drug should be associated with a copious fluid intake to avoid nausea and vomiting. It is very important that only freshly prepared solutions of the drug be used. Pentamidine isethionate, a new preparation, is well tolerated. The individual dose for an adult is calculated on the basis of 4 mg. per kilogram of body-weight. A course of daily injections for ten days is recommended.

*Treatment of Later Stage.*—If the case is seen in the later stages, especially when the cerebrospinal system is invaded by the trypanosome, then suramin is not alone sufficient, and a combined treatment with tryparsamide is indicated. A preliminary course of 5 gm. of suramin is given as above, and after an interval of a week or ten days, depending on the condition of the patient, tryparsamide injections are begun. The initial dose is 1 gm. in 10 c.c. of freshly prepared double-distilled water injected intravenously. The next dose is 2 gm., and the later doses may have to be increased to 3 gm., depending on the stage of the disease. The injections may be given twice weekly till a total of 24 gm. have been administered. The dosage of tryparsamide for children is 0.07 gm. per kilogram of body-weight; 0.055 gm. per kilogram for young adolescents; and 0.045 gm. per kilogram for adults. For children, suramin may be given in doses of 0.4 to 0.6 gm. Children tolerate this drug well.

Recent work has shown that the therapeutic efficacy of tryparsamide is due to its conversion into a trypanocidally active trivalent form of arsenic in the course of its passage through the body tissues. Chemical determination of the amount of arsenic in the cerebrospinal fluid shows that it reaches its maximum concentration fourteen hours after administration, and that this rapidly decreases during the next forty hours.

*Toxic Effects of Drugs.*—At the end of the course of 5 gm. of suramin, some signs of irritation of the kidneys are often observed, as indicated by a temporary albuminuria with a few granular casts in the urine. This usually clears up quickly. A toxic dermatitis not infrequently appears, but this also disappears on cessation of the treatment. Tryparsamide may produce ocular symptoms in some patients, *e.g.*, photophobia, lachrymation, pain in the eyes and dimness of vision. Hence, in every case, before beginning treatment with tryparsamide, the eyes should be carefully examined, especially in the fields of vision and the fundus oculi. The tryparsamide itself should be a very pure preparation, made up fresh each day in sterile double-distilled water. In suspicious cases the drug should be stopped and an intravenous injection of Ametox (May & Baker) given. It is put up in 5 c.c. ampoules containing 0.45 gm. of thiosulphate of soda, and should be injected on alternate days till six injections have been given. B.A.L. (British Anti-Lewisite) has proved an efficient specific in the treatment of the toxic effects of arsenical therapy (see p. 216). Other toxic effects of tryparsamide, *e.g.*, the Herxheimer reaction and the nitritoid reaction, are rare in the treatment of trypanosomiasis. Diamidines may produce toxic symptoms varying from slight flushing of the face, itching—especially of the genitalia, nausea and dyspnoea, to severe collapse associated with a steep fall in blood pressure. Late symptoms, two to eight months after completion of treatment by stilbamidine, are paræsthesia, anæsthesia and hyperæsthesia along the course of the trigeminal nerve, which may last for eighteen months to two years.

*Drug Resistance.*—It has been shown that trypanosomes become readily drug-fast to the arsenicals. Moreover, these drug-fast strains retain this property even after passage through the tsetse fly. This opens up a question of great importance in connection with the prevention of the disease. Although the trypanosome can be rendered drug-fast to suramin, this, fortunately, occurs much less frequently than with arsenicals; hence the value of the treatment with suramin and, probably, the diamidines, described above.

**General Management.**—An important preliminary to specific therapy is the disinfestation of the patient of helminths, *e.g.*, ancylostomes, bilharzia, etc., as will be described later.

During the earlier stages of the treatment the patient may be kept in bed, but the later courses of tryparsamide may be given at the out-patient clinic. The diet should be as generous as possible, if the digestion is not impaired. In the later stages of untreated cases the patient will be completely bedridden and will have to be fed and nursed; fortunately, this stage is not so frequently seen nowadays owing to the great advance in methods of treatment.

During the course of treatment it is advisable to make examinations at regular intervals of the glandular and spinal fluids, the dose being adapted in accordance with the results of the examinations.

**Personal Prophylaxis.**—*Chemoprophylaxis.*—It has been found that a single intravenous dose of suramin will give protection for 115 days. It is particularly applicable to infections with *T. rhodesiense*. It is claimed that a single dose of 150 to 200 mg. of pentamidine gives protection for six months and possibly for a year.

*Avoidance of Flies.*—Flies bite during the middle of the day; thus, by avoiding the fly belts in the daytime, the individual can protect himself against infection. Tsetse flies, except *Glossina swynnertoni*, are not found in dwelling-houses as a rule. For protection against *G. swynnertoni* the same precautions in dwelling-houses should be instituted as for malaria (see p. 278).

## LEISHMANIASIS

### KALA-AZAR

**Specific Therapy.**—*Drugs Employed.*—Pentavalent compounds of antimony: Pentostam (B. W. & Co.); Stibatin (Glaxo); Urea stibamine, introduced by Brahmachari of Calcutta; trivalent compounds of antimony, such as tartar emetic (sodium-antimony tartrate); Stilbamidine; Pentamidine.

*Treatment of Acute Attack.*—Excellent results have been obtained from British organic compounds of antimony such as Pentostam (B. W. & Co.), Stibatin (Glaxo) and Urea stibamine.

Pentostam is a stable solution containing the equivalent of 100 mg. of pentavalent antimony in each cubic centimetre. It is issued in boxes of ten ampoules of 6 c.c. each. It can be given either intravenously or intramuscularly. For the adult four injections of 6 c.c. are given on four consecutive days. This initial course causes a prompt fall of temperature and a general improvement of health. After a rest of from ten to fourteen days 6 c.c. may be given on each of two successive days to complete the treatment. In very debilitated subjects the initial dose may be reduced to 2 c.c. A reduced dose should also be given in cases which have recently undergone treatment with antimony in another form. In some cases the course may have to be repeated. For stibatin a similar course is indicated.

Urea stibamine dissolved in sterile doubly distilled water is given intravenously in doses of 0.1 gm. increasing by 0.05 gm. up to a maximum of 0.25 gm. For adults a total quantity of 2.6 gm. is given in twelve doses over a period of thirty-two days. For children proportionately smaller doses are given.

Tartar emetic (sodium antimonyl tartrate) is still used, and it has the advantage of being cheaper than the other compounds. A sterile 2 per cent. solution in fresh double-distilled water is prepared. An initial dose for an adult is 2 c.c., and this is gradually increased to 5.8 c.c., which is the maximum individual dose for an adult. It is injected slowly intravenously. For young children, in whom intravenous medication is difficult, a dose of 12 mg. in 60 c.c. sterile saline may be given intraperitoneally in the middle line of the abdomen just below the umbilicus. The injections are given bi-weekly and the total dose for an adult is 30 gr. (1.8 gm.). It is very important that the solutions should be made up daily as required, with fresh double-distilled water, as they are liable to undergo deterioration on standing.

Urea stibamine and tartar emetic are highly irritant to the subcutaneous tissues. It is therefore most important to ensure that the needle of the syringe is actually in the vein before beginning the injection.

The introduction of stilbamidine marked an advance in the treatment of kala-azar, and antimony resistant cases respond favourably to it. It has been found particularly valuable in the treatment of kala-azar in the Sudan, where antimony preparations have proved disappointing. Weight for weight about a quarter as much stilbamidine is required per case as neostibosan. Stilbamidine is given very slowly intravenously in doses of 1 mg. per kilogram of body-weight for adults. Young children tolerate the drug proportionately better than adults. Adam and Yorke treated two adults successfully with a total dosage of 360 and 400 mg. respectively. Other workers recommend a larger total dose up to one gramme or even more. It is very important that only fresh solutions should be used, as the solution undergoes a change when exposed to light and this greatly increases its toxicity. Its therapeutic value is unfortunately greatly diminished on account of the serious neuropathy which follows its administration in a high percentage of cases (see p. 246).

*Treatment of Relapse.*—Some cases become resistant to the drug that is being used, in which case it is advisable to change to one of the other preparations of antimony. Where the relapse takes the form of a skin lesion, called dermal leishmanoid or post-kala-azar leishmaniasis, it will usually be found that the patients have suffered from visceral kala-azar about a year previously and have been insufficiently treated with antimony. Biopsy of the skin shows the presence of the Leishman-Donovan body. They respond well to courses of treatment as described above, using pentostam, stibatin or urea stibamine; for this reason it is very important to recognize the true nature of the skin lesion.

*Toxic Effects of Drugs.*—An early sign is coughing, and a feeling of constriction in the chest may occur immediately after, or even during, an intravenous injection of antimony. This is an indication for the reduction of the subsequent dose. In some cases vomiting and purging may develop during the course of treatment, the symptoms being not unlike those of cholera. Towards the end of the course cramps in the muscles of the leg may be felt and occasionally arthritic pains are experienced. A finely punctate rash may appear after courses of 4:4 diamidino stilbene. Jaundice may also be noted occasionally. If toxic symptoms arise, the drug should be temporarily discontinued. Occasionally the patient is unable to tolerate a sufficient quantity of the drug to ensure destruction of the parasite. For the toxic effects of stilbamidine see p. 246. To avoid them the fluid

intake should be considerably increased during the administration of the drug.

**General Management.**—The expulsion of helminths and the treatment of coincident infections, such as malaria, are very important. The anæmia should be treated with full doses of iron (see p. 470). In very severe cases a blood transfusion may be indicated.

The appetite in cases of kala-azar is generally unimpaired and the digestion is good, so he should receive a nourishing, well-balanced diet with plenty of fluid in the form of glucose lemonade. He should be kept in bed and carefully nursed during the acute phase. Cancrum oris should be treated by penicillin cream (see p. 93).

**Personal Prophylaxis.**—*Chemoprophylaxis.*—So far this has not been employed in kala-azar.

*Other Methods of Protection from Infection.*—Domestic and personal cleanliness is important. In some areas dogs are also infected, so any infected animals should be destroyed. Mosquito curtains of a fine mesh and repellents, as indicated in malaria (see p. 245), should be used to prevent the bites of sand-flies. It is an advantage to live in the upper storey of the dwelling, as sand-flies do not usually leave the lower parts of the house.

### ORIENTAL SORE

**Specific Therapy.**—*General.*—The antimony preparations already mentioned are used in the same way as for kala-azar.

*Local.*—Berberine sulphate, which is put up by May & Baker as a 2 per cent. solution in ampoules under the name of "orisol," is given in doses of 2 to 3 c.c., injected at points round the periphery of the sore. Two to three such injections at weekly intervals are usually sufficient to cure the sore. Alternatively 3 c.c. of a mepacrine solution (0.1 gm. in 5 c.c. of sterile water) are injected at three sites round the sore. The procedure is repeated twice weekly. Treatment with X-rays, ionization and carbon dioxide snow have all been recommended, as has the scraping of the sore with a Volkmann spoon, followed by the application of pure carbolic, after which the sore is covered with elastoplast. Berberine or mepacrine injections are the most effective treatment and should be tried initially, but if not successful the other alternatives may be employed.

**Personal Prophylaxis.**—As for kala-azar.

## SPIROCHÆTOSIS ICTEROHÆMORRHAGICA

(Weil's Disease)

**Specific Therapy.**—If the diagnosis is made within seven days of the onset the injection of 30,000 units of penicillin three-hourly with a total dosage of 1,000,000 units (see p. 89) is of value, and has largely replaced the polyvalent serum which used to be employed in early cases. In advanced cases in which jaundice and uræmic symptoms have developed, no specific treatment is effective.

**General Management.**—As the liver is generally severely attacked, glucose in orange or lemon juice should be given freely by the mouth or by intravenous drip if necessary.



The patient should be kept at rest and carefully nursed. A milk diet should be given in the early stages. If vomiting is marked, nutrient enemata may be required and 10 minims (0.58 c.c.) of 1 : 1,000 adrenaline in a little water may be given by the mouth. The prevention and treatment of oliguria or anuria has been described on p. 244.

**Personal Prophylaxis.**—All food should be carefully protected from contamination by rats, which are the carriers of the parasite. The urine and faeces of patients should be disinfected and the hands of the attendant should be carefully sterilized, and if abrasions are present on the hands, rubber gloves should be worn. Swimming, especially using the "crawl" stroke, in bathing pools, canals or rivers suspected of being the source of infection should be avoided.

Infectious jaundice may be regarded as a disease of certain industries. Sewer workers, miners, fish curers and workers in certain sugar-cane plantations are particularly liable to become infected and should be warned to take special precautions, *i.e.*, protect their food and drink from the excreta of rats and to protect themselves from abrasions. Weil's disease in Britain now comes under the Workmen's Compensation Act and is notifiable in Scotland but not in England or Wales.

The Japanese have used—with success—killed cultures of the *leptospira icterohæmorrhagiæ* as a prophylactic. This is probably unnecessary in this country.

## RAT-BITE FEVER

(*Sodoku*)

**Specific Therapy.**—*Drugs Employed.*—Neoarsphenamine and penicillin.

**Treatment of Acute Attack.**—Neoarsphenamine is given intravenously in doses of 0.4 to 0.6 gm. dissolved in 10 c.c. of sterile double-distilled water. One dose is sometimes sufficient to effect a cure, but as a rule it is necessary to repeat the injections on several occasions at short intervals. Penicillin has given good results in the treatment of the spirillar form of the disease and it may be useful in preventing relapses.

Recently a form of the disease due to *streptobacillus moniliformis* has been treated successfully with penicillin when arsenicals have failed.

**Treatment of Relapses.**—Some cases may relapse, but, fortunately, this is rare. A case seen by the author continued to have relapses over a long period, in spite of repeated courses of neoarsphenamine, and died from a complicating pneumonia. In this case the parasite had become drug-fast. In such cases a course of bismuth injections might be tried (*vide* Yaws, p. 263).

**General Management.**—A bite by a rat, ferret or cat should be cauterized by pure carbolic after the wounds have been freely opened up.

During the attack of fever the patient should be kept in bed on a light diet.

**Personal Prophylaxis.**—Protection against bites by rats, cats or ferrets. As in plague, the most important protection against this disease is efficient rat destruction.

## PLAGUE

**Specific Therapy.**—In plague, specific therapy plays a less prominent part in the treatment than in the other diseases discussed. There is no specific drug, the two specific agents employed being antisera and bacteriophage.

Recently a potent serum has been prepared in the Bombay laboratory which has given promising results in some cases. Injections should be begun early in the disease and given intravenously in doses of 30 to 40 c.c., repeated as required.

Bacteriophage is injected into the bubo in doses of 2 to 3 c.c. on the first day and again on the second. In septicæmic cases 3 c.c. or more have been given intravenously. A preliminary injection of 5 to 10 c.c. of the patient's own blood (autohæmotherapy) is recommended.

**Non-specific Therapy.**—Recent experimental work has shown the remarkable efficacy of sulphonamide drugs, particularly sulphadiazine. The initial dose for an adult is 4 gm. followed by 1 gm. four-hourly for thirty-six hours, the dose being subsequently reduced. In severe cases of septicæmic plague or when, on account of vomiting, administration by the mouth is contraindicated, a 3 c.c. ampoule of the sodium salt, containing 1 gm. of the drug, may be administered intramuscularly or intravenously, diluted to 10 c.c. with normal saline. A large fluid intake during treatment should be encouraged. For pain and sleeplessness, the injection of  $\frac{1}{4}$  gr. (16 mg.) of morphia is indicated. It is important to accelerate the bursting of the bubos, for when this occurs the general symptoms improve and there is less risk of the blood becoming infected. Frequent poulticing is useful, and as soon as softening occurs the bubo should be incised. In view of the recent experimental work and the experience gained in the treatment of war wounds, the cavity of the bubo may be packed with sterile sulphonamide powder, using 5 to 15 gm. of the drug. No gauze is used in packing. The powdered drug is simply blown into every part of the cavity. Indolent bubonic swellings may be treated with liniment of iodine.

**General Therapy.**—This is a very important factor in the treatment of the various forms of plague, of which nursing forms a large part. In the earlier stages tepid sponging and the application of ice caps for the high fever and headache are indicated. Sponging the body every hour is a much safer method of lowering the temperature than the employment of antipyretic drugs.

**Personal Prophylaxis.**—The most important measure is prophylactic inoculation with Haffkine vaccine. A dose of 4 c.c. is given to an adult. The dose is reduced for children. No unnecessary visits to a person suffering from plague should be made, and areas in which plague is occurring should be avoided. Nurses should be careful to cover any abrasions which they have on their skin, and those engaged in plague duty should wear protective clothing impregnated with repellents (see p. 277) to prevent access of infected fleas. Attendants on cases of pneumonic plague should be inoculated with anti-plague vaccine. They should wear masks of absorbent cotton-wool (16 cm. by 12 cm.) enclosed in muslin and retained by a many-tailed bandage and, in addition, goggles and rubber gloves. All houses should be made rat-proof and sprayed with D.D.T. (see p. 277).

## UNDULANT FEVER

### MELITENSIS TYPE

**Specific Therapy.**—In this disease there are no specific drugs available. Autogenous vaccines and a serum marketed by Mulfords have been used. The serum may be given intravenously in doses of 50 to 100 c.c. in the early

stage of the disease and may be repeated at twenty-four-hour intervals. At a later stage, the vaccine can be employed. Starting with a dose of 10 to 15 million organisms, it may be increased gradually till a dose of 200 million is reached.

**Non-specific Therapy.**—Recently sulphathiazole given early in full doses (see p. 74) has seemed to have had a beneficial effect in some cases. Compounds of antimony, *e.g.*, pentostam and stibatin, have been used to cut short the recurrences of the fever. Four intramuscular injections of pentostam may effect a cure in some cases of undulant fever (for dosage see Leishmaniasis, p. 247). In resistant cases protein shock therapy should be given a trial, using T.A.B. vaccine, starting with a dose of 10 to 15 million and working up to 100 million. Brucellin, a culture filtrate, has given encouraging results. 0.1 c.c. is given to test for sensitivity, and, if no marked systemic reaction occurs, 0.2 c.c. is given intradermally and 0.8 c.c. intramuscularly some hours later. Thereafter four intramuscular injections of 0.8 c.c. are given at three-day intervals.

**General Therapy.**—This is very important. Careful nursing is essential in this usually long-drawn-out illness. The nurse should be instructed to keep the temperature below 103° F. (39° C.) by sponging with tepid water and vinegar, which is more efficacious than the use of antipyretics. If hyperpyrexia threatens, the wet pack or cold bath should be used. For pain and sleeplessness, morphia may be employed, but care must be taken that a habit is not formed by too continued use. Clothing should be frequently changed if there is much sweating. Diet should at first be composed of milk, orange juice, glucose and marmite soup, and then gradually increased. Care must be taken to avoid overfeeding. Plenty of fluid should be taken. Rest in bed for at least three weeks after the temperature has become normal should prevent a relapse.

**Personal Prophylaxis.**—As the chief method of spread is by milk (goat's milk in the case of the *melitensis* type, and cow's milk in the *abortus* type), all milk in endemic areas should be boiled before use. Unfermented cheese is also a frequent but unsuspected source of infection and should be avoided. Man is probably naturally more resistant to the *abortus* than the *melitensis* type. Prophylactic injections of dead vaccines have been tried with encouraging results for both types.

### ABORTUS TYPE

Treatment is on the same lines as for the *melitensis* type, but protein shock therapy has given particularly good results in cutting short the *abortus* infection.

### CHOLERA

**Specific Therapy.**—There is no specific treatment for cholera, hence non-specific therapy has to be employed and has been developed on scientific lines.

**Non-specific Therapy.**—The very serious symptoms of cholera are mainly due to profound dehydration of the tissues. Consequently, it is most important to replace the fluid and salt as rapidly as possible, or the case will end fatally in a very short time. The scheme of treatment recommended by

Rogers in a moderately severe case is as follows: first the blood pressure and specific gravity of the blood are estimated. The latter is quite easily carried out. A series of small bottles can be purchased containing glycerin and water, the specific gravity of which increases by two degrees in each bottle from 1,048 to 1,070. The finger is pricked and the blood is sucked into a capillary pipette. A drop is added to each bottle, and the bottle in which the drop remains stationary in the middle of the fluid for a minute or two gives the specific gravity of the blood. The normal specific gravity of the blood of a European is 1,058 and that of an Eastern native is 1,056. A specific gravity of 1,063 in cholera indicates a fluid deficiency requiring an injection of 3 to 6 pints of saline to restore it to normal. A systolic blood pressure below 70 mm. is a very serious sign. The fluid is best replaced by using a hypertonic saline solution containing the following: 120 gr. (7.2 gm.) of sodium chloride; 6 gr. (0.4 gm.) of potassium chloride; 6 gr. (0.4 gm.) of calcium chloride; 1 pint of sterilized water. This is injected by the intravenous route; owing to the collapsed state of the veins it will be necessary to expose the vein and insert a cannula. If the rectal temperature is below 99° F. (37° C.), the saline should be heated to 100° F. (37.8° C.). If it is above 100° F. (37.8° C.), the solution should be given at a temperature between 80° and 90° F., as there is a risk of hyperpyrexia. The fluid is run in at the rate of not more than 2 oz. per minute; if there is distress or headache, it should be slowed down to 1 oz. per minute. From 3 to 6 pints should be administered, the amount being controlled by the specific gravity of the patient's blood. If the specific gravity rises and the blood pressure falls, it will be necessary to repeat the transfusion. In severe cases several transfusions may be required. If there is a tendency to suppression of urine, a rectal or intravenous injection of hyperalkaline solution should be given—sodium bicarbonate, 150 gr. (9 gm.) to 1 pint of isotonic saline, to be given slowly and repeated if necessary in cases where collapse has been overcome but suppression persists. At the same time the patient should be encouraged to drink water freely, and calcium permanganate may be added to the water so that it is just slightly pink in colour (see also treatment of anuria in blackwater fever, p. 244). The administration of a plasma drip transfusion between the periodic saline infusions still further reduces the mortality in cholera. A suspension of 7 oz. of kaolin in 14 oz. of water may be given in 1-oz. doses at frequent intervals even if there is vomiting, as it helps to adsorb the toxin. Morphine may be required if muscular cramps are very painful. Recently the use of sulphaguanidine (see p. 76) has been shown to improve considerably the results of treatment.

During the stage of reaction, should purging persist, large doses of salicylate of bismuth may be useful. At this stage, if the skin temperature rises above 103.5° F. (39° C.) or the rectal temperature above 104° F. (40° C.), cold sponging should be carried out.

Pregnancy is a serious complication of cholera, as the foetus almost invariably dies of toxæmia. Lovell in the Philippines reduced the mortality rate by watching for evidence of death of the foetus or commencement of abortion; he then removed the foetus. Pneumonia is a further serious complication.

Bacteriophage has been employed in the treatment of cholera. In an acute case its action will not be sufficiently rapid, so that it cannot replace the use of hypertonic saline, but it may be a useful adjuvant. A polyvalent

bacteriophage may be given in drachm (4 c.c.) doses by the mouth every thirty minutes till symptoms improve, or 5 c.c. may be given intravenously along with the hypertonic saline. This form of therapy in cholera, and in some other diseases, has aroused interest and requires mention.

**General Management.**—*During the Acute Phase.*—Nursing is very important during this stage. The patient should be kept strictly in the horizontal position in a warm bed and in a well-ventilated room. The surface heat should be maintained by hot-water bottles, or warmed bricks placed alongside the feet, legs and flanks. The patient must not be allowed up to pass his stools, but a warmed bed-pan should be available. The foot of the bed should be raised. All food should be withheld for some hours whilst the disease is active. Nurses must see that all discharges, soiled linen, etc., are disinfected with a  $2\frac{1}{2}$  per cent. cresol solution.

*During Convalescence.*—Alcohol may be of benefit to those accustomed to it. Great care is necessary in beginning to give food for fear of producing a relapse. To begin with, farinaceous foods such as arrowroot, cornflour and milk whey should be given, and this diet should be continued until the kidneys act freely. The recumbent position should be enforced for about two weeks to avoid sudden cardiac failure. Convalescence, however, is usually surprisingly rapid.

**Personal Prophylaxis.**—Inoculation with a dead cholera vaccine has been widely employed with good results. The initial dose of 0.5 c.c., given subcutaneously, should contain 4,000 million cholera vibrios. The second dose of 1 c.c. should be given ten days later. Bacteriophage has also been recommended as a prophylactic, and if this is used, 30 c.c. of potent bacteriophage should be added to the well (see note above). During cholera epidemics great care should be taken to maintain the general health. All attacks of diarrhoea should be treated at once. Purgatives, especially salines, should be avoided. All drinking water and milk should be boiled. All food should be protected from flies, and uncooked vegetables, as well as raw and unripe fruit, should be avoided. The hands should be washed before eating, and food and drinking utensils cleaned in boiling water. Visits to cholera districts should if possible be postponed.

## AMŒBIC DYSENTERY

**Specific Therapy.**—*Drugs Employed.*—Emetine and its various preparations (alkaloid of ipecacuanha), chiniofon, diodoquin, carbarsone and acetarsol.

*Treatment of Acute Attack.*—The best treatment is to begin at once subcutaneous injections of 1 gr. (0.06 gm.) of emetine hydrochloride dissolved in 1 c.c. sterile distilled water. This dose is given daily for seven days, or it may be given in divided doses of  $\frac{1}{2}$  gr. (0.03 gm.) morning and evening. Emetine bismuth iodide (made up in gelatin capsules) by the mouth, combined with irrigation of the bowel with chiniofon, is given after the emetine injections. At 8.30 A.M., after a cleansing enema of sodium bicarbonate, 8 oz. of a  $2\frac{1}{2}$  per cent. chiniofon solution is run into the bowel and the patient encouraged to retain it as long as possible. At 9.30 P.M. a sedative, such as 1 gr. (0.06 gm.) of phenobarbitone, is given. At 10 P.M. 1 gr. (0.06 gm.) of emetine bismuth iodide is administered; later this dose may be increased to 2 gr. (0.12 gm.). It is not necessary to give more than a total of 19 gr. (1.14 gm.) in about twenty-one days. The last food and drink should have

been taken at 6 P.M. Some vomiting and diarrhoea may be expected and are not contraindications. Alcohol in any form should be prohibited. Such a combined course of treatment tends to prevent relapses.

*Treatment of Relapses.*—A preliminary eight-day course of penicillin (see p. 89) and sulphasuxidine (see p. 76) is given. This is followed by a twelve-day course of emetine bismuth iodide and chiniofon retention enemata as described above. The patient should then take two pills each containing 0.2 gm. of diodoquin thrice daily for one month. Carbarsone, an organic arsenic preparation, may then be given. It has the additional advantage of being non-toxic. The average daily adult dose is  $7\frac{1}{2}$  gr. (0.45 gm.), and this should be given for ten days. A course of acetarsol has also been found very useful in resistant cases. 2 gr. (0.12 gm.) are given thrice daily with each meal for a week. All treatment is then omitted for a week, and thereafter half a tablet is administered thrice daily for another week. This course should be repeated after a fortnight's interval.

In some persistent cases it may be necessary to perform cæcostomy and irrigate the large bowel daily with  $2\frac{1}{2}$  per cent. chiniofon solution. The wound is kept open till the lesions in the bowel are completely healed, as determined by sigmoidoscopic and X-ray examination. Ileostomy is preferable, as it puts the large bowel at complete rest. The risk of all surgical measures in this condition is, however, very considerable.

*Toxic Symptoms.*—Emetine affects the heart and may cause fibrillation if given in excessive doses or for too long a time. Neuritis may be produced, and in some cases paralysis of the diaphragm and intercostal muscles may occur with serious respiratory embarrassment. The skin may show a fine brawny desquamation and the finger-nails an atrophic condition with marked increase in the size of the lunule. Emetine is particularly toxic in bacillary dysentery when it is administered in cases which have been wrongly diagnosed. This toxic action occurs easily in young children, and emetine should be administered to them with the greatest care.

*General Management.*—*During the Acute Phase.*—Nursing is most important during the acute phase. As already noted, emetine is a toxic drug, and during its administration the patient should be kept in bed under supervision. The mouth should be carefully washed out and any excess of saliva removed. The patient should not be allowed to get out of bed to pass a stool, but a bed-pan should be used. The diet should consist of easily digested food having a low residue—milk, rice, orange-juice glucose, baked apples, tea and toast.

*During Convalescence.*—The patient may be allowed to get up to go to the bathroom. The diet may be gradually increased, but potatoes, carrots, etc., should be used sparingly. It is not necessary to starve the patient. The best guides are the appetite and tongue of the patient. Alcohol should be forbidden for a month or two after treatment is completed.

*Tests of Cure.*—These consist of palpation of the region of the cæcum and ascending colon for signs of tenderness and thickening, the sigmoidoscopic examination of the bowel and the examination of the stools for *Entamæba histolytica*. Such tests are carried out a month after completion of treatment and thereafter at intervals of four months up to sixteen months.

*Personal Prophylaxis.*—As the infection is acquired through food or drink contaminated by cysts of *Entamæba histolytica*, precautions must be taken to prevent this. In areas where the disease is endemic, food should be care-

fully protected from flies; all milk and water should be boiled before consumption. Uncooked vegetables should be avoided. In areas where amebiasis is prevalent considerable protection may be obtained by taking two pills (0.2 gm. each) of diodoquin three times daily for twenty days.

### COMPLICATIONS OF AMOEBIC DYSENTERY

**Amoebic Hepatitis.**—For this the best treatment is a course of injections of emetine hydrochloride for ten days as for amoebic dysentery. If the diagnosis is correct, the symptoms quickly clear up with this treatment, but if they do not, then at the end of this time the diagnosis must be revised. The course is frequently used in this condition as a "therapeutic diagnosis."

**Amoebic Liver Abscess.**—When symptoms suggest the presence of pus it is necessary—in addition to the administration of emetine—to explore the liver, and, if pus is found, to evacuate it by aspiration. For this purpose, a full-sized aspiration needle is used, as the pus is thick. Local anaesthesia should be employed. In the absence of localizing signs, the best point to insert the needle is in the right anterior axillary line in the eighth or ninth interspace. The needle should be introduced inwards and slightly upwards for 3 to 3½ in. At least six explorations in different directions in the liver should be made before abandoning the attempt to find pus. If pus is found, the needle is connected up with a Potain's aspirator and the pus evacuated. A further ten-day course of injections of emetine is then given. The combination of aspiration and administration of emetine is by far the best method of dealing with a liver abscess, and the earlier these are carried out the better. In some cases it may be necessary to do an open operation either by the trans-peritoneal or pleural route. The drawback to this, in the hot moist climate of some parts of the tropics, is that there is a very great risk of the abscess cavity becoming secondarily infected, though the danger is now lessened by the prompt use of penicillin. When a liver abscess opens through the lung, the pus may be completely evacuated by the patient coughing it up. In some cases the drainage may fail, and in these cases surgical measures are indicated.

**Pulmonary Amebiasis.**—This condition is not secondary to liver abscess. The infection has been conveyed by the blood stream to the lungs from the primary lesion in the large intestine, causing broncho-pneumonia. These cases respond very rapidly to a course of emetine.

**Amoeboma of Colon and Rectum.**—This rather rare but very important complication produces a granulomatous tumour of the colon and rectum which may be mistaken for carcinoma. In the case of a person returned from the East (it may be after a considerable interval) in whom a tumour in these sites is detected, the possibility of an amoeboma should be kept in mind. A course of penicillin and emetine treatment as described above should be given. The tumour should disappear *completely* if it is an amoeboma. This is important because amoeboma and carcinoma of the bowel may co-exist. Surgical measures may be required for acute obstruction or perforation of the bowel.

Patients who have suffered from any of the above complications should not, if possible, return to the tropics. Before permission to return is given, tests of cure as described above should be made, and if necessary a further course of treatment given.

## LAMBLIASIS

*Giardia (Lambli) intestinalis* is a protozoan parasite, and numerous observers have brought forward evidence of its pathogenicity. Others deny this, since it has been found in the intestine of a large percentage of normal children in England and Canada. It can also be demonstrated in duodenal juice and bile removed by Einhorn's tube. It is associated with a type of recurring diarrhoea accompanied by abdominal distension. The stool resembles that found in sprue.

Mepacrine acts almost as a specific against this parasite. One tablet of 0.1 gm. is given thrice daily after food for five to ten consecutive days, with proportionately smaller doses for children. Acetarsol has also been employed and has proved to be an effective drug in this condition, especially in cases where the parasite is located in the duodenum. The dosage is one to two 4-gr. (0.24 gm.) tablets daily for six days. A high protein dietary has been recommended during treatment. If severe diarrhoea is present, bismuth salicylate may be given in drachm (3.88 gm.) doses thrice daily. It has to be remembered that this parasite is extremely difficult to eradicate, and repeated courses of treatment may be required.

## THE SPRUE SYNDROME

### *Tropical Sprue, Idiopathic Steatorrhœa, Celiac Disease*

The onset of the syndrome usually occurs insidious<sup>7</sup>, but occasionally may be acute and sudden. The presenting features in a typical case are (1) steatorrhœa, (2) loss of weight and strength, and muscular wasting, (3) abdominal distention and flatulence, (4) anæmia, (5) clinical features resulting from inadequate absorption of vitamins and minerals, *e.g.*, glossitis, stomatitis, osteoporosis, tetany, a tendency to bleed, etc. Skeletal defects and slowing or cessation of growth are features particularly found in celiac disease. Although defective absorption of fat is the abnormality most easily recognized, it must be remembered that the absorption of water, sodium chloride, glucose, vitamins and minerals is also impaired. The absorption of amino acids, however, is little affected, a point of practical importance in the dietetic management of the case. The excretion of bile and pancreatic ferments is not affected. No organic obstruction to their excretion or to the absorption of nutrients from the small intestine has been found at autopsy. The cause of the failure in absorption in the sprue syndrome is unknown, but it is possibly conditioned by the lack of some factor which may be a vitamin or a hormone which is necessary for the functioning of an enzyme system connected with fat absorption.

Treatment will be described under the following headings:—

1. General Management.
2. Diet.
3. Drugs, including vitamins, liver extracts and glandular preparations.
4. Maintenance Treatment.

**General Management.**—Sprue patients are very susceptible to chills. In the acute stage of the illness they should be nursed in bed and kept warm.



This usually causes a considerable reduction in the degree of diarrhoea. Intercurrent infections induce relapses and every attempt should be made to guard against them and to treat them promptly and efficiently. Nursing is important and the nurse must supervise the special diet and keep accurate records of the body-weight and the number and character of the stools.

**Diet.**—The basis of the sprue diet is that it should be low in fat and high in protein. Carbohydrates, especially in the form of starchy foods, should be moderately reduced, the degree of reduction being assessed by the degree of frothy fermentation of the stool. Until recently it was the custom to treat sprue cases with a series of step-ladder diets whose basis was the rigid exclusion of fat in the initial stages by the use of de-fatted milk protein in the form of skimmed milk powder or sprulac (Cow & Gate). A small addition of orange juice and calf's-foot jelly was allowed. The amount of protein was progressively increased every few days as improvement occurred. Such diets were unappetizing and initially low in calories. The introduction of folic acid (see p. 486) has made it possible to give a more adequate and pleasant diet from the start because of the dramatic improvement which occurs within two or three days of the institution of folic acid therapy. In most cases of the syndrome as it occurs in adults it is possible to prescribe safely an initial diet containing approximately 50 gm. of fat, 100 gm. of protein and 200 gm. of carbohydrates. With further improvement the protein can be raised to 120 to 150 gm. The fat and carbohydrates should be increased very cautiously as it is only by trial and error that the quantities which can be tolerated can be ascertained. In regard to protein foods, mention has already been made of the value of milk protein. Lean meat, chicken, fish and eggs, especially white of eggs, are well tolerated and can be introduced into the diet from the beginning in small amounts. Liver, tender and lightly cooked, or in the form of liver soup, has been recognized for centuries as of particular value. Boiling, baking, grilling and roasting are the methods of cooking to be employed, but not frying. Fruits—apples, oranges, tomatoes and strawberries—are allowed and should be served initially in the form of purées, jellies or juices. Green and yellow vegetables, if tender and well cooked and passed through a sieve, may be permitted in small quantities. Rich starchy foods (cereals and potatoes) and concentrated sugary foods (canned fruits, dried fruits, sweets, etc.) must be prohibited in the initial stages of treatment because intolerance to them may be as marked as to fats. Intolerance to monosaccharides may be less than to polysaccharides, and small amounts of glucose can be used for sweetening. When improvement in the diarrhoea has occurred the patient may be permitted to take one or two thin slices of toast or rusks with each meal and thereafter the quantities of cereals and potatoes may be cautiously increased to the limits of tolerance. Milk fats are well tolerated and the patient on folic acid may be permitted to take whole milk in place of skimmed milk. Cream should not be given and the amount of butter limited to one ounce or less daily, depending on the patient's ability to absorb fats. Articles to be avoided completely during the initial stage of treatment are overdone and twice-cooked meats; foods cooked or fried in fat; condiments such as pepper, mustard, chillies, sauces, chutneys, curries and spiced foods; duck, salmon, trout, mackerel and herring; new bread; salad dressings and sauces of all kinds; suet puddings; cakes with icing; raisins and pastry; sweets and chocolate; alcoholic drinks and aerated water.

**Drugs.—Folic Acid.**—The introduction of synthetic folic acid to the practice of medicine in 1945 greatly simplified and improved the treatment of tropical sprue and to a less extent idiopathic steatorrhœa. Unfortunately clinical experience suggests it is of little value in cœliac disease. Folic acid should be given orally in doses of 20 mg. daily for fourteen days, when the dose can be reduced to 10 mg. or even less daily. Within five days of starting treatment in a case of tropical sprue the number of motions will fall to one or two daily, abdominal distension and flatulence rapidly improve, nausea and anorexia are relieved, and a gain in strength and weight quickly follows. Glossitis and stomatitis, usually held to be evidence of deficiency of nicotinic acid and riboflavin, likewise clear up rapidly. While equally dramatic results may be obtained in some cases of idiopathic steatorrhœa, in others little or no improvement occurs. No satisfactory explanation is available for these divergent therapeutic results unless it be that in non-tropical forms of the syndrome irreversible changes are produced in the alimentary tract consequent on a long continued state of malnutrition.

The effect of folic acid on the anæmia is variable. In cases with severe anæmia and a megaloblastic bone marrow a satisfactory response similar in character and magnitude to that obtained in pernicious anæmia usually results, and the blood picture may be restored qualitatively and quantitatively to normal. In many cases, however, although the anæmia is macrocytic in character, the bone marrow picture is predominantly normoblastic. In such cases folic acid may be ineffective in restoring the blood count to normal and parenteral and oral liver therapy must be given. If there is a hypochromic or dimorphic anæmia, iron must be administered in the usual dosage (see p. 470). Despite the remarkable improvement resulting from folic acid in the general state of health and in the control of diarrhœa, there is evidence to show that the absorption of fat is little benefited, at least for some time. This finding clearly indicates the need for continued restriction of fat even in the state of remission in the majority of cases.

**Liver and Liver Extracts.**—The value of raw and cooked liver and liver soups in the treatment of sprue has been recognized for a long time prior to the introduction of folic acid. There is evidence to suggest that liver or liver extracts given orally are more effective than parenteral liver therapy. More recently parenteral liver therapy has been shown to have a good effect on the clinical manifestations of sprue even in cases in which it failed to improve the blood picture. The dosage required in sprue is two or three times greater than that used in pernicious anæmia (see p. 479). It is generally believed that the so-called "crude liver extracts" such as Campolon are more effective than the refined preparations such as Anahæmin, although this view is not accepted by certain leading authorities including Wintrobe. Sufficient time has not elapsed since the introduction of folic acid to assess the future place of parenteral liver therapy in the treatment of sprue. At the time of writing it is justifiable either to give combined liver and folic acid therapy, or to assess first the effects of treatment with folic acid alone and then to administer liver extracts if the results of folic acid therapy are not entirely satisfactory. Oral liver preparations including proteolyzed liver should always be tried in cases refractory to parenteral liver therapy or folic acid.

**Bile Salts, Pancreatic Extracts, Hydrochloric Acid.**—Since biliary and

pancreatic function is normal in sprue, there seems to be no logical reason for prescribing bile salts or pancreatic preparations although these have been commonly recommended in the past. Gastric secretion is normal in two-thirds of the cases of the sprue syndrome and accordingly a supplement of dilute hydrochloric acid is unnecessary. Even when achlorhydria is present it is questionable whether the administration of hydrochloric acid in pharmacological doses is of any value (see p. 467).

*Vitamins.*—It is doubtful whether the routine administration of supplements of a variety of vitamins is any longer justified in view of the rapid relief of all symptoms which follow treatment with folic acid and liver extracts. Aneurin, riboflavin and nicotinic acid will relieve the appropriate symptoms resulting from their deficiency in sprue but have no curative effect on the diarrhoea, abdominal distension and loss of weight and strength. They have no influence in improving the absorption of fat. If prescribed at all they should only be given during the short initial period while awaiting the effects of folic acid treatment. Adequate supplies of vitamins, both fat and water soluble, can thereafter be obtained from a properly balanced diet. Yeast has been strongly recommended by various authorities, not only because it is a valuable source of members of the vitamin B complex but because it has been claimed to exert a more favourable influence on fat absorption than either folic acid or liver extract. It may be given in moist or dried form in doses up to 1 oz. daily. When osteoporosis, defective growth or rickets are present, as in coeliac disease, supplements of calcium and vitamin D are indicated. For tetany the treatment is the same as that described on p. 415. Occasionally a hæmorrhagic state develops which is resistant to all forms of treatment other than blood transfusion and vitamin K. For the treatment of hypoprothrombinæmia see p. 512.

*Sulphonamide Drugs.*—There were many reports from India during the Second World War of the value of sulphaguanidine in the treatment of sprue in the severe relapse stage when diarrhoea is severe and the stools are often very watery. Whether the condition would not have responded more effectively to folic acid is uncertain as the vitamin was not available in India during the war. Sulphaguanidine is also recommended for a similar relapse state in coeliac disease which unfortunately may be resistant to both folic acid and parenteral liver therapy.

*Other Drugs.*—Chalk, kaolin, charcoal and codein, which were frequently employed in the past for the control of diarrhoea and flatulence, are not so often required when folic acid is used, and then only for a few days while awaiting its action. Patients in the severe relapse state with frequent watery motions develop dehydration and marked deficiency of sodium chloride due to the great loss of fluid and salt in the stools. This must be counteracted by an adequate intake of fluid and salt.

*Maintenance Treatment.*—The individual variation in response to treatment varies so greatly in different cases that no general rules can be laid down. Each case must be considered on its merits. The prognosis is better in tropical sprue than in idiopathic steatorrhœa or coeliac disease. Some cases of the sprue syndrome can be completely cured and require no dietetic regulation or maintenance treatment, while others remain in a state of chronic invalidism with steatorrhœa and marked muscular weakness despite all forms of treatment. In between these extremes lie the majority of cases who do well on the lines of treatment discussed above but have to be careful

for the rest of their lives in avoiding dietary indiscretions, current infections, chill and excessive physical and psychological fatigue. Many of these cases remain well with dietetic regulation alone, while others require maintenance treatment with folic acid or liver extract in varying quantities given periodically or continuously. The dosage can only be determined by careful assessment of each individual case. For maintenance purposes it is advisable to supplement folic acid with liver therapy since patients who are controlled by folic acid alone are apt to develop peripheral neuritis. In the past it has been recommended that patients who have had tropical sprue should not return to the tropics if possible. It is doubtful if this recommendation is valid with the modern methods of treatment now available.

## LEPROSY

**Specific Therapy.**—In recent years it was thought that in chaulmoogra oil and its derivatives we had a specific remedy for leprosy, but further experience has not confirmed this view. The position of the treatment of leprosy is very similar to that of tuberculosis. No one measure is sufficient, but a general building up of the patient's resistance by diet, improved personal hygiene, etc., is of the greatest value. Chaulmoogra oil has a place in this treatment. It is a very old remedy for leprosy in India, the best oil being obtained from the seeds of the *hydnocarpus wightiana*. The oil itself is used and has the advantage of being both cheap and effective. Moogrol (B. W. & Co.) is a mixture of the esters of the acids of the Chaulmoogric series for intramuscular injection. When iodized by the addition of 0.5 per cent. iodine it is much less irritating. Alepol (B. W. & Co.) or sodii hydnocarpus is a mixture of the sodium salts obtained from the less irritating low melting fractions of the acids of *hydnocarpus wightiana* oil. It is a recent preparation and much cheaper than the ethyl esters. Two doses given weekly for one year cost only two shillings. A good method of administration is to inject the oil intradermally into the skin lesions. The oil should be prepared from the fresh seeds, as it is important to avoid the products of decomposition, which are very irritating. The oil is fairly stable. Its viscosity is lessened if it is mixed with 4 per cent. creosote and injected warm (45° C.). It is advisable to give multiple small doses intradermally with a short needle, care being taken not to pierce the subcutaneous tissue. A small wheal is raised round each injection. An area of 12 sq. cm. may be infiltrated at one sitting, and this can be done rapidly by a trained operator. The course is begun with small doses, 0.05 to 0.1 c.c., and gradually increased till 6 c.c. or more are administered. The injections are given once weekly. A rise of temperature, associated with swelling and redness of skin nodules and thickening of nerves, may occur. Such reactions are treated by keeping the patient in bed, administering a purge and 0.02 to 0.04 gm. of sodium antimonyl tartrate intravenously in 2 c.c. sterile distilled water. Septic foci should be looked for and treated. After the reaction has subsided the subsequent dose of chaulmoogra oil should be limited to 0.5 c.c., which should thereafter be increased as before.

Moogrol is given in doses of 1 c.c. intramuscularly and this is increased up to 5 to 6 c.c. At the same time iodicin (B. W. & Co.) tablets are given. The dose is 0.25 gm. per 100 lb. (45 kg.) of body-weight and this is increased every two weeks up to 1 gm. per 100 lb. Alepol is given intra-

venously. If an equal quantity of blood is mixed with it in the syringe before injection, thrombosis of the vein is prevented. As severe reactions may in some cases follow intravenous injections, it is well to commence with intramuscular or subcutaneous doses of 1 c.c. of a 3 per cent. solution (increased by 0.5 to 5 c.c. or more) twice weekly. The intravenous injections of 1 c.c. of a 1 per cent. solution may be given alternately with the intramuscular injections.

It is advisable to control the injection of chaulmoogra oil and its derivatives by observations on the blood sedimentation rate. A high reading indicates an active lesion and caution should be adopted in administering the oil.

Diasone (di-sodium formaldehyde sulfoxylate) has been favourably reported on in the treatment of leprosy. It is given orally in capsules of 0.3 gm. A course of treatment lasts for two to four years. It starts with 0.3 gm. of diasone or 0.5 gm. of sulphetrone every second day. The dose is doubled after a week, and then very gradually increased till a maximum of 2 gm. of diasone or 3 gm. of sulphetrone are given daily. If anæmia is present it should be treated, and specific treatment should not be started till the hæmoglobin percentage is over 70. Sulphone drugs, diasone and sulphetrone, are likely to replace chaulmoogra oil in the future.

Protein shock therapy has been tried and found useful. T.A.B. vaccine is given intravenously, commencing with a dose of 5 to 10 million, repeating it twice weekly with increasing doses until a 100-million dose is reached—or more if reactions are insufficient. In the neuritic form of the disease it has been suggested that there is a vitamin B<sub>1</sub> deficiency and injections of this are recommended (see p. 398). Surgical measures of various kinds may be required, *e.g.*, eye operations, tracheotomy, removal of dead bone, amputations, etc. If a single small lesion of the skin exists, less than 1 cm. in diameter, unassociated with other lesions, the obvious treatment is excision along with general treatment carried on over a long period. The appearance of patients with large nodules can be improved by applying a curved clamp and shaving off the tissue above. The stump is then treated with pure carbolic acid. Perforating ulcers in leprosy are very resistant to treatment; dead bone should be removed. A chronic ulcer without much discharge may be improved by infiltration round its edge with chaulmoogra oil. Ulcers of the nasal cavity should be treated, after the removal of crusts, by the application through a speculum of trichloroacetic acid or chromic acid (1-10), or by diathermy. These procedures should be carried out under a local anæsthetic of cocaine and adrenaline. Diasone clears up the nasal lesions quickly.

The neuritis of leprosy should be treated by relaxing and not by stretching the nerve. Occasionally constricting bands have to be divided surgically. Cold abscesses of the nerves should be incised and contents scraped out after the nerve sheath has been split; drainage is seldom necessary.

Considerable involvement of the eye may be present without obvious clinical signs. The eye should be examined after administration of atropine in all cases of leprosy of the face and nose. Diasone has given good results in the treatment of lesions of the eye.

It is very important to locate and remove foci of septic infection and dental treatment is important. Various forms of physiotherapy are often

useful in relieving nerve pains, restoring muscular function and healing ulceration. It is essential to recognize and treat complicating infections, e.g., particularly syphilis (see p. 210). Intestinal parasites should be dealt with; malaria, kala-azar and any other infection must be treated.

**General Management.**—Patients should be encouraged to come at the earliest opportunity for treatment and warned that this must necessarily be prolonged and that final recovery depends to a large extent on their co-operation. Treatment must be continued till all active signs of the disease disappear and repeated bacteriological examination of the skin and nose are negative. It is advisable after this to keep the patient under observation and warn him that a relapse may occur.

Scrupulous and systematic attention must be paid to personal and domestic hygiene and cleanliness; frequent bathing and free use of soap; changes of underclothing; good food; fresh air; exercise; light work; avoidance of fatigue—all these points should be insisted upon. Europeans who have contracted leprosy invariably show improvement on return to a more bracing climate from the tropics. It should be noted that improvement frequently occurs without the administration of any drug when the patient is placed under favourable conditions, hence great care is necessary in assessing the value of a drug in the treatment of leprosy.

**Personal Prophylaxis.**—As children are much more susceptible to infection than adults, they should always be removed from leprous parents and from all contact with lepers. Leper colonies with facilities for modern treatment, and run on humanitarian lines, are very important for the prophylaxis of leprosy. Particular care should be taken to disinfect the nasal discharge of lepers and also their eating and drinking utensils. Contact with discharging lesions of the skin should be strictly avoided, as these often contain very large numbers of bacilli. Native washermen, cooks and other servants should be carefully and regularly inspected for any signs of leprosy, and, if found to be infected, should be suspended from their work and put under treatment. Treatment with diasone, as described above, is particularly valuable in this connection as the patient becomes non-infectious by this means more rapidly than with any other treatment.

## YAWS

**Specific Therapy.**—*Drugs Employed.*—Arsphenamine; neoarsphenamine; acetarsol; carbarsone; sodium-bismuth tartrate; injection of bismuth (B.P.); bismuth arsanilate; bismuth arsphenamine sulphonate; penicillin.

*Treatment of Early Stage.*—The best treatment is a daily injection of 100,000 units of penicillin in beeswax and oil up to a total of at least 1,000,000 units followed by a combination of arsenic and bismuth. In the tropics the natives improve so rapidly with the first few doses of the arsenicals that they often do not return for completion of the course, and only appear when a relapse sets in. Neoarsphenamine is given intravenously to adults, but may be given to children intramuscularly suspended in oil if the intravenous route is not possible. The initial dose for adults is 0.6 to 0.9 gm. in 10 c.c. sterile distilled water. For children under two years the dose should be 0.1 gm., and for those up to ten years old it should be 0.3 gm. It may be given intramuscularly, alternating with bismuth in weekly injections. In

this way severe reactions are avoided. The dose of sodium-bismuth tartrate for an adult is 3 gr. (0.18 gm.) dissolved in 3 c.c. sterile distilled water or in oil; for children up to two years,  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.); from two to eighteen years, 1 to 2 gr. (0.06 to 0.12 gm.). A course of about twelve weekly injections, alternating neoarsphenamine and bismuth, may be considered suitable for the treatment of a case of yaws. Stomatitis may be avoided if the bismuth is injected into the deep subcutaneous rather than the muscular tissue. The other bismuth preparation, injection of bismuth (B.P.), which is metallic bismuth suspended in glucose solution, is given weekly into the deep subcutaneous tissue in doses of 3 gr. (0.18 gm.), with a total of 60 gr. (3.6 gm.) in refractory cases. The following are given orally: acetarsol, starting with a dose of two 4-gr. (0.24 gm.) tablets for an adult, and increasing to three on the second, and four on the third day: miss a day and repeat in reverse order. The dose for children is  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.). It is said to cause slight diarrhoea, but it is a convenient method for mass-treatment. Carbarsone is another drug given by mouth in gelatin capsules (pulvules). The average dose for an adult is  $7\frac{1}{2}$  gr. (0.45 gm.), which may be given daily for ten days. The course may be repeated after a short interval. The treatment by injection described above is, however, to be preferred to the oral method.

*Treatment of Relapse.*—In cases which relapse, a second course of the combined treatment will be required.

**General Management.**—For the painful “crab” yaws of the feet a local application of a 2 per cent. tartar emetic ointment in vaseline is very useful. The name is given because the patient walks like a crab on account of the lesion in the feet. Perchloride of mercury solution (1 : 1,000) may be used to cleanse the sores.

The general health should be improved by good food. Sufferers from yaws are almost invariably undernourished and an improvement in their nutrition may in itself be sufficient to bring about recovery in early cases. Daily bathing and stimulation of the skin by abundance of demulcent drinks are also helpful, and in the colder season warm clothing is indicated.

Helminthic and other complicating infections should be treated.

**Personal Prophylaxis.**—The protection of wounds and abrasions from infection by contact, or by flies, is the most effective measure. Public bathing places liable to pollution by discharges should be avoided.

## YELLOW FEVER

**Specific Therapy.**—There are no specific drugs for this disorder, and serum from convalescents, even if available, is of no value when symptoms have developed.

**Non-specific Therapy.**—Yellow fever is caused by a virus and the infection varies in severity from a mild one with no recognizable clinical signs to an extremely severe illness characterized by classical symptoms. Mild cases are usually detected after recovery in the course of serological surveys in tropical America and Africa; the serum in such cases gives a positive mouse protection test and recovery has occurred as the result of a rapid and complete development of spontaneous immunity without treatment. In

a severe case the principles of treatment are (1) complete rest in bed; (2) an ample supply of fluids and carbohydrate; (3) alkalies used in small quantities with discretion; (4) the administration of calcium to prevent guanidine intoxication.

Rest in bed is most important and it is better that a patient taken ill even in unfavourable conditions should be made reasonably comfortable where he is rather than that the risky procedure of transporting him to a more suitable environment should be undertaken. If the patient is restless and sleepless,  $\frac{1}{4}$  gr. (16 mg.) of morphia can be given. At the beginning of the illness a mild saline purgative is necessary, but thereafter constipation should be treated by enemata. The patient should be given plenty of fluids to drink made up with the juice of citrus fruits and glucose. Hypoglycæmia and liver damage may be combated by the administration of an intravenous drip of 5 per cent. glucose saline, if facilities are available for this procedure. To combat acidosis 10 to 15 gm. of sodium citrate or bicarbonate may be given daily by the mouth in divided doses, but if there is much vomiting 15 gm. sodium bicarbonate in one pint of sterile water may be given intravenously. The associated guanidine intoxication is said to be relieved by the administration of 5 gm. daily of calcium lactate given orally, or 10 c.c. of a 10 per cent. solution of calcium gluconate intravenously. Anuria is a very serious complication, and for its treatment on the lines described on p. 244 must be begun early. For the first few days solid food is contraindicated, though, as mentioned above, glucose drinks may be given freely, and it may be necessary to administer glucose intravenously. More solid foods should be introduced very gradually, and a normal intake is not well tolerated till the temperature becomes normal. Should the temperature rise above 103.5° F. (40° C.), cold sponging should be employed. Convalescence should be prolonged and resumption of activity carefully regulated.

**Personal Prophylaxis.**—Yellow fever vaccine is the most important personal prophylactic. All persons going to yellow fever areas in tropical America or Africa should receive prophylactic treatment with it, and indeed travellers are not granted permits to proceed to such areas unless they produce a certificate of vaccination done at least ten days previously. The vaccine now in use is an attenuated living yellow fever virus made from eggs with seven-day embryos which have been inoculated with the virus. It is issued in ampoules in dried form, and for immediate use a sufficient quantity of sterile normal saline is added to produce a volume of approximately 0.5 c.c. for each dose. It is injected subcutaneously. The earlier batches of the vaccine which were made with human serum produced hepatitis in a number of cases two or three months after inoculation. The present vaccine is not made with human serum and cases of hepatitis have ceased. The only after-effects noted are allergic reactions in persons hypersensitive to egg and chick protein. Recently 600,000 persons in Columbia were immunized with the vaccine, and failure was recorded in one case only—a boy who developed yellow fever five days after the inoculation—while there were many cases of yellow fever in the uninoculated population. The vaccine is effective for at least four years. A complete list of centres where inoculation is undertaken in this country is given below.

As yellow fever is mosquito (*Aedes*) borne the personal prophylactic measures as detailed on pp. 245, 278 are necessary.



## LIST OF CENTRES FOR YELLOW FEVER PROPHYLACTIC INOCULATION

A circular issued by the Crown Agents for the Colonies, 4 Millbank, London, S.W. 1, gives the following list of centres for inoculation:—

LONDON. Wellcome Research Institution, 183-193 Euston Road, N.W.1.

LIVERPOOL. Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, 3.

NEWCASTLE. Regional Blood Transfusion Centre, 78 Jesmond Road, Newcastle-on-Tyne, 2.

LEEDS. Regional Blood Transfusion Centre, Nearwood Park Colony.

OXFORD. Regional Blood Transfusion Centre, New Pathological Department, Radcliffe Infirmary.

BRISTOL. Regional Blood Transfusion Centre, Southmead Hospital.

CARDIFF. Regional Blood Transfusion Centre, 19 Newport Road.

BIRMINGHAM. Regional Blood Transfusion Centre, 17 Highfield Road.

EDINBURGH. Bacteriological Department, Edinburgh Royal Infirmary, Edinburgh, 3.

ABERDEEN. City Hospital, Aberdeen.

GLASGOW. Public Health Clinic, 20 Cochrane Street, Glasgow, C. 1.

DUNDEE. Bacteriological Department, University of St. Andrews.

DUBLIN. Trinity College, Dublin.

BELFAST. Emergency Hospital, Musgrave Park, Balmoral, Belfast.

No fee is charged for the inoculation and issue of the official certificate, except in London and Liverpool, where a nominal fee of 5s. is charged. In the case of Dublin and Belfast a higher fee may be charged. Practitioners can arrange an appointment for their cases, at suitable times, by letter or telephone.

## RABIES

Cases of rabies present themselves for treatment when the symptoms of the disease are already manifest, or because they have been recently exposed to infection by the bite of a rabid animal. In the former, a fatal termination invariably occurs and treatment is only palliative.

**Palliative Treatment of the Developed Case.**—The violent and painful spasms may be best controlled by inhalations of chloroform. Subcutaneous injection of curare may be tried, using tabloid hyp. curarinæ chloride (B. W. & Co.).  $\frac{1}{120}$  gr. (0.5 mg.) up to a maximum of  $\frac{1}{2}$  gr. (0.03 gm.). When swallowing becomes impossible, rectal alimentation is required. Nurses should do all they can to reassure the patient and allay fear and excitement.

**Treatment of those who have been Exposed to Infection.**—Local treatment is most important and the sooner it is undertaken the better is the outlook for the patient. The wounds caused by rabid animals should be opened up freely so that access may be gained to every part, and pure carbolic acid applied. Carbolic acid is better than nitric acid as it is not so painful and it destroys the virus. It has been shown that irrigation of the bites with a 20 per cent. solution of soft soap is as effective as cauterization with fuming nitric acid—perhaps even more so—and is readily available in an emergency. If this treatment is carried out within an hour of the exposure, the risk of contracting rabies is slight. The most serious bites are those on the face. An animal which has bitten a person and is suspected to be rabid should not be killed, but kept securely under

observation. If it is alive and well ten days later, it is very unlikely to have been suffering from rabies at the time it bit the person, and the latter is therefore not at risk. Persons who have been licked on the unbroken skin or on abrasions, which are not recent, are not in danger.

After the local treatment has been applied, and if the person is definitely at risk, he should undergo a course of anti-rabic inoculations. The nature of the vaccine may be briefly indicated here. First, a fixed virus is prepared; this is done by injecting an emulsion of the brain of a rabid dog intracerebrally into a rabbit. When the rabbit dies, some of its brain is injected intracerebrally into a second rabbit, and so on through a succession of rabbits until the virus becomes exalted and kills the rabbit in exactly ten days; the virus is now known as the "fixed virus" and is used for the preparation of the vaccine. Some strains of the virus have better antigenic properties than others; for example, it was found that a fixed virus obtained from Paris was a better antigen than one that had been in use in India for some time. There have been various methods of preparing the vaccine with the fixed virus, and the technique has gradually evolved. At present a dead carbolized virus is commonly employed. This is made by emulsifying the brain of an infected rabbit, or sheep, in 1 per cent. carbolic saline. This is allowed to stand in the incubator for twenty-four hours at 37° C. to kill the virus. The strength of the brain emulsion may be from 1 to 5 per cent. The former being used in the less severe cases and the latter for severe bites about the face and head, which require intensive treatment. The course usually lasts fourteen days, daily injections of 4 c.c. of the vaccine being given subcutaneously on each side of the abdomen. During the course the patient is instructed to abstain from all alcohol and vigorous exercise. These precautions are very important, and if not taken the treatment may prove ineffective and the patient die of rabies. In a small percentage of cases certain "accidents," as they are called, may occur during the treatment, *e.g.*, paraplegia, a condition like Landry's paralysis, etc. They are rare and the mode of production is not clear. The carbolized vaccine has reduced the frequency of these unfortunate occurrences. The vaccine can be sent by mail, and application can be made to local health authorities in Britain for a supply and for instructions for use.

**Personal Prophylaxis.**—All animals suspected of rabies should be avoided. Dogs showing signs of choking should be handled with great care, as this is often the first sign of rabies, and fingers should never be put into the mouth of the dog. Muzzling is important, especially if cases of rabies in dogs are occurring.

## TROPICAL NEURASTHENIA

Tropical life may exaggerate a neurotic predisposition and physical diseases of the tropics may manifest themselves in neurasthenic symptoms. Far too often the medical man does not know what neurasthenia is and tells the patient there is nothing the matter with him and that all that is required is for him to "pull himself together." Such advice is usually ill-advised. The patient feels ill and his doctor cannot find out what is the matter with him, and so he thinks he must have a very obscure malady which is incurable. If an infection, *e.g.*, malaria, dysentery, etc., is detected, the patient should be instructed as to the nature of the tropical disease

and should be assured that with suitable treatment he will improve quickly. This will allay his anxiety. If, after dealing with exciting and predisposing causes, there is no definite improvement, then long leave to a good climate must be prescribed. Alcohol probably plays a more important part than climate in causing neurosis in the tropics, and therefore it should be forbidden. Smoking, if carried to excess, should be reduced or prohibited. If insomnia is marked it should be treated by such measures as a hot bath and a cup of hot milk at bedtime, or, if necessary, mild hypnotics such as butobarbital, two tablets of  $1\frac{1}{2}$  gr. (0.09 gm.) half an hour before retiring. Hobbies should be encouraged, such as golf, fishing, etc., which will distract the patient's attention from himself and take him into pleasant surroundings in the fresh air.

It is very important to seek carefully for any underlying infection, and if found treat it thoroughly.

**Prophylaxis.**—Certain types of individuals never adjust themselves to tropical conditions and are very liable to develop this form of anxiety neurosis. In examination of recruits for work in the tropics it is necessary for the medical examiner to have had considerable tropical experience and to have paid particular attention to the reaction of individuals to tropical environment. It is not easy to lay down definite rules, but particular attention should be paid to the family and personal history. The recruit should be asked to fill up a form stating: (a) whether he has ever suffered from fits; (b) whether he, or any member of his family, has ever been treated in a mental hospital or suffered from a "nervous breakdown"; (c) what standard he reached at school; (d) what is the longest time he has ever held any one job. Independent reports on the character and conduct of the applicant may be helpful. It is useful to give the layman going to the tropics simple instruction in the principles of tropical medicine and hygiene.

## HELMINTHIC INFECTIONS

### SCHISTOSOMIASIS

**Specific Therapy.**—*Drugs Employed.*—Tartar emetic (sodium antimonyl tartrate); emetine; "hypoloid" stibophen (Burroughs Wellcome & Co.); anthiomaline (May & Baker).

*Treatment of an Acute Attack.*—Tartar emetic is given intravenously. For convenience it may be put up in a sterilized vaccine bottle with a rubber cap in a strength of  $\frac{1}{2}$  gr. (0.03 gm.) to 1 c.c. of double-distilled water. For use, dilute each centimetre with 5 c.c. sterile double-distilled water. The technique is the same as that described in the treatment of kala-azar (see p. 247). The injections are given on alternate days and the dose gradually increased till 2 to  $2\frac{1}{2}$  gr. (0.12 to 0.15 gm.) are given at one injection. The total amount of tartar emetic required for a course is 25 to 30 gr. (1.5 to 1.8 gm.). For children, 10 gr. (0.6 gm.) is sufficient for a course with a maximum of 1 gr. (0.06 gm.) for a single dose. The course will occupy four to six weeks. Recently an intensive course of treatment has been employed with success. Two grains (0.12 gm.) of sodium antimonyl tartrate dis-

solved in 5 per cent. glucose saline are given intravenously at 9 A.M. and noon and 1 gr. (0.06 gm.) at 3 P.M. on two consecutive days. It is of fundamental importance to give the injections very slowly at the rate of 2 c.c. per minute. "*Hypoloid*" *stibophen* is given intramuscularly and therefore is convenient for administration to children. It is put up in a 7 per cent. solution in ampoules and the dosage recommended for an adult is: first day, 1.5 c.c.; second, 3.5 c.c.; third, 5 c.c.; fifth, 5 c.c.; seventh, 5 c.c.; ninth, 5 c.c.; eleventh, 5 c.c.; thirteenth, 5 c.c.; fifteenth, 5 c.c. For children the initial dose should be 0.5 c.c. rising to 2 to 3 c.c. according to age. *Anthiomaline* (May & Baker), which can be given by intramuscular injection, has been recommended for the treatment of schistosomiasis in adults and children. It is supplied in 2 c.c. ampoules of a 6 per cent. solution, each cubic centimetre containing the equivalent of 0.01 gm. of antimony metal. Injection may be given every second day, commencing with 1 c.c. and increasing by 1 c.c. until the average adult dose of 4 c.c. is reached. Thereafter injections of 4 c.c. should be given (three in a week) until a total dose of 50 c.c. is reached and repeated examinations have demonstrated complete elimination of the parasite. The dose for a child of twelve would be approximately half the adult dose, commencing with 0.5 c.c. and increasing to 2 c.c. Children tolerate the drug well. *Emetine* can be given to children who are intolerant to antimony, or whose veins are too small for intravenous therapy. It is given intramuscularly and the initial dose should not exceed  $\frac{1}{2}$  gr. (0.03 gm.), and a maximum dose for a child is 1 gr. (0.06 gm.) and the total for a course is 15 to 20 gr. (0.9 to 1.2 gm.). The heart must be carefully watched during treatment with emetine.

*Treatment of Relapses.*—Relapses generally occur if the full course of treatment has not been completed. When they do occur, the treatment outlined above must be repeated. The author recently saw a case of urinary schistosomiasis showing marked resistance to antimony treatment. In explanation of resistance to antimony Khalil points out that persons vary greatly in their rate of excretion of the drug. Those whose excretion is exceptionally quick are resistant to treatment and have to be given a series of courses. Those whose excretion, on the other hand, is unduly slow are liable to poisoning, which may even prove fatal.

*Toxic Symptoms.*—The toxic symptoms of the antimony preparations and emetine have already been described in connection with leishmaniasis and amœbic dysentery (see pp. 248, 255). The specific therapy is applicable to all three forms of schistosomiasis, *viz.*, *schistosoma hæmatobium* (urinary form), *schistosoma mansoni* (intestinal form) and *schistosoma japonica* (Far Eastern schistosomiasis).

*Control of Treatment.*—Regular cystoscopic and sigmoidoscopic examinations are important. An intradermal test with cercarial antigen has been shown to be of value as a test of cure.

*Non-specific Therapy.*—In the urinary form, stone and papillomata of the bladder require to be removed by operation. Hyperplasia of the vagina and cervix is best treated by scraping. In the intestinal form with extensive papillomata of the rectum, removal of the whole tube of mucous membrane is recommended—as much as 12 to 15 in. (30 to 37 cm.) have been successfully removed. There is little tendency to contraction of the rectum, and control of the anal sphincter is regained. When splenomegaly is a marked feature, as is frequently the case, splenectomy for so-called Egyptian splenomegaly

is recommended. In the late stage of the Far Eastern variety, hepatic cirrhosis becomes a marked feature and little can be done when this stage is reached (see Cirrhosis, p. 589).

**Personal Prophylaxis.**—In endemic areas, drinking from or bathing in rivers, ponds and canals should be avoided. Children should be carefully and repeatedly warned about this. Sportsmen also should be warned against wading, especially when snipe shooting, in infected localities; even fishing in canals in Egypt is not free from risk. All drinking water should be boiled. The reason for these precautions is to avoid infection from snails harbouring the parasite. The schistosome undergoes part of its life-cycle in certain species of fresh-water snails from which the parasite emerges in the form of actively swimming cercariæ, and when they meet the human host they infect him by penetrating through his skin or mucous membrane. Benzyl benzoate has the important property of repelling the cercariæ. By the use of gloves and stockings impregnated with it, invasion of the skin by cercariæ can be prevented (see p. 278).

## CESTODIASIS

### TÆNIA SAGINATA

**Specific Therapy.**—*Drugs Employed.*—Felix mas, which is the rhizome of the male fern; tetrachlorethylene and oleum chenopodium.

*Treatment of Intestinal Form.*—The adult worms are present in the intestine and the following scheme of treatment for an adult is recommended. Preliminary partial starvation is essential for two days. Food should be restricted to weak tea and a little toast; for clearing out mucus from the bowel, 20 gr. (1.2 gm.) of sodium bicarbonate should be given thrice daily. In the morning sodium sulphate ( $\frac{1}{2}$  oz.) is given. Fresh extractum filicis liquidum is put up in gelatin capsules containing 15 minims (0.9 c.c.) in each. On the day of treatment at 8 A.M. give two capsules of 15 minims (0.9 c.c.), repeat at 8.30 A.M. and 9 A.M. The dose for an adult male is  $1\frac{1}{2}$  drachms (5.3 c.c.), for a female, 1 drachm (3.5 c.c.). The patient must then lie perfectly quiet in bed sipping water. At 10.30 A.M. give sodium sulphate ( $\frac{1}{2}$  oz.). When the bowels move freely, segments of the worm begin to appear. They must all be carefully preserved and a search made for the head. In cases where the filix mas has failed to eradicate the entire worm, a useful anthelmintic is a combination of tetrachlorethylene and oil of chenopodium in the following mixture:—

R	Tetrachlorethylene	.	.	.	.	3.5 c.c.
	Ol. Chenopod.	.	.	.	.	1 c.c.
	Paraff. Liq.	.	.	.	.	28 c.c.

Adults should receive a full dose; children under six, 2 drachms (7 c.c.); up to eight years the dose should be 3 drachms (10.5 c.c.); and up to fourteen, 4 drachms (14 c.c.). The mixture should be made up fresh. After half an hour the patient is given sodium sulphate ( $\frac{1}{2}$  oz.).

If the head has not been recovered, efforts should be made to prevent the further growth of the helminth, and for this purpose 15 gr. (0.9 gm.) of  $\beta$ -naphthol in 5-gr. (0.3 gm.) tablets should be taken first thing in the morning on an empty stomach for ten days.

**Personal Prophylaxis.**—As the ox is the intermediate host of *T. saginata*, beef for consumption should be very carefully cooked.

**TÆNIA SOLIUM***(Cysticercosis)*

Normally the cysticercus stage of *Tænia solium* takes place in the pig, but sometimes the development occurs in man with very serious results, as it selects for its location the muscles and the central nervous system in particular, causing epilepsy and other manifestations varying with the location of the parasite. The cysticerci, when they become dead and calcified, can be demonstrated in the tissues by X-ray examination; before calcification, cysts under the skin may be felt on palpation, excised and submitted for examination. Unfortunately the treatment of this condition is very unsatisfactory and is purely symptomatic. For the epilepsy, phenobarbitone and phenytoin may be given as in the case of idiopathic epilepsy (see p. 875). Unless there are very definitely localizing signs, surgery is not indicated.

**Personal Prophylaxis.**—This is very important. A patient with intestinal tapeworms should be treated thoroughly and at once, since he may acquire the visceral form of cysticercosis if he harbours *T. solium* in his intestine. As the pig is normally the intermediate host of *T. solium*, the flesh—particularly in the East—(where the disease is very common amongst them)—should not be eaten unless it has been obtained from a well-supervised slaughter-house and has been thoroughly cooked. Raw vegetables should be avoided, as in the tropics they are frequently contaminated with the eggs and ripe segments of tapeworms. Nurses and attendants should handle with great care the ripe segments of *T. solium* and take every precaution to avoid infection of their hands and food.

**TÆNIA ECHINOCOCCUS GRANULOSUS***(Hydatid)*

The sexually mature worm occurs in the dog as the definite host and is a small tapeworm. Man is its intermediate host and in him it may form large cysts in various organs, particularly in the liver and lungs. Aspiration should not be attempted either for diagnosis or treatment, as the fluid is often under great pressure and is toxic; further, it contains scolices which, if they escape, may disseminate the disease widely in the tissues. Drug therapy is valueless and surgical treatment by open operation is the only method indicated. In the case of the liver, the incised cyst may be stitched to the abdominal wall and allowed to fill up by granulating (marsupialization). Aspiration of cysts is dangerous because fluid may escape suddenly from a pulmonary cyst into the lungs, or into the peritoneal cavity from a cyst in the liver, and in the former case death from suffocation may result. The fluid which escapes into the tissues is toxic and symptoms of collapse, or even death, may result. An open operation with adequate drainage is therefore required. Penicillin is useful when cysts are infected.

**Personal Prophylaxis.**—Close contact with the sheepdog, the host of the adult worm, must be avoided. After handling the sheep, whose wool may be infected, the hands should be carefully washed, especially before eating.

## FILARIASIS

**Specific Therapy.**—Recently it has been shown that the pentavalent compounds of antimony can kill the adult worms, particularly *F. bancrofti*. (For details of dosage see p. 247.) The microfilaria are not affected by the drug and do not disappear from the circulation till about three months after completion of treatment. The principal types of filarial infections are *Filaria bancrofti*, *Filaria Malayi* and *Filaria loa* (Loa Loa).

**Non-specific Therapy.**—The *bancroftian* and *Malayan infestations* may produce a series of clinical manifestations which require treatment. The principal of these are:—

*Filarial lymphadenitis, lymphangitis, orchitis and funiculitis.* In the acute stage the treatment is rest in bed with elevation of the parts. Calamine lotion should be applied, and in cases of fever hydrotherapy is useful. A careful search should be made for bacterial septic foci. Autogenous vaccines made from the vesicles in the skin have been found useful in combating the secondary bacterial infection. Sulphonamides and penicillin have been employed to treat the secondary bacterial infections in these cases. Favourable results have followed the administration of sulphathiazole in dosage of 0.5 gm. given every four hours till symptoms abate. As secondary bacterial infection may play a considerable part in the various forms of filarial lesions, there will be an extensive field for sulphonamide and penicillin therapy.

*Filarial Abscess.* Pus should be evacuated, hot boracic fomentations applied and a course of penicillin given.

*Lymph scrotum, hydrocele and varix.* Surgical measures are required in these cases. Suspensory and pressure bandages are useful.

*Elephantiasis.* Again a careful search should be made for focal infections. Non-specific shock therapy is of value in these cases and T.A.B. vaccine should be given intravenously, commencing with doses of 5,000,000 to 10,000,000, increasing gradually up to 100,000,000. The limb should be carefully guarded against injuries and elastoplast bandages may be found helpful. The limb should be massaged and kept elevated. Various operative procedures have been proposed, but none are entirely satisfactory. Kondoleon's operation consists of free incision of the fascia lata of the leg and removal of a large section of aponeurosis; this assists the anastomosis of lymph channels and veins.

*Synovitis.* This is not an uncommon complication of filariasis, and as there may be no very evident trauma to account for it, the condition may be rather puzzling, especially if it occurs in this country. The treatment is on the usual lines for synovitis.

*Chyluria.* This is not an unusual complication and the treatment should consist of rest in bed with the foot of the bed elevated. Restriction of fats and fluids in the diet, gentle purgation and the washing out of the bladder with warm boracic lotion should all be carried out. If blood is present in the urine the following mixture may be used for irrigation:—

R	Liq. Adrenal. Hydrochlor. (B.P.)	.	fl. dr. i (3.5 c.c.)
	Zinc Sulph.	.	gr. v (0.3 gm.)
	Lot. Acid. Boric (B.P.C.)	.	ad fl. oz. i½ (35.5 c.c.)

To be used with equal quantities of warm water.

**Personal Prophylaxis.**—In practice this amounts to anti-mosquito measures and protection from mosquito bite—as have been detailed under malaria (see pp. 245, 278).

### FILARIA LOA

(*Loa Loa*)

The condition known as Calabar swellings is caused by this worm. Specific treatment should consist in a trial of pentavalent antimony preparations. (For details of administration see p. 247.) Should the adult worm appear under the conjunctiva or skin, it may be removed. There are generally a number of worms. For the relief of the swelling an injection of 1 c.c. of adrenaline (1:1,000) is useful. An abscess may be produced by a dead worm. The pus should then be evacuated and hot boracic dressing applied. Occasionally the worm moves in the subcutaneous tissue to near the larynx and may give rise to the serious complication of oedema glottidis, in which case a tracheotomy will be required at once.

**Personal Prophylaxis.**—Protection is required against the bites of the vector, a horse-fly (*Chrysops dimidiata*) which comes into houses and bites during the daytime. Therefore the dwelling-houses in endemic areas should be protected with wire gauze and by the use of D.D.T. and repellents (see p. 277).

### OTHER FORMS OF FILARIASIS

**Dracunculus Medinensis or Guinea Worm.**—The adult female worm is found in the subcutaneous tissue, generally of the leg. In the early stages the patient may suffer from urticaria, vomiting and purging due to toxins produced by the worm. There is a marked eosinophilia. These symptoms are frequently very puzzling, as the existence of the worm may not be obvious. The injection of 1 c.c. of adrenaline (1:1,000) frequently gives relief. Later the worm penetrates the skin and the diagnosis is clear. A simple form of treatment is to tie a small piece of silk thread to the worm as it protrudes from the opening of the skin. The thread is attached to a piece of stick. The worm is then wound round the stick daily with very gentle traction; if too much force is applied, it may rupture the worm and a disastrous cellulitis may result. Fairley has devised an operation for removal of the worm *en masse* at once. If cellulitis and other septic complications have occurred, then these should be dealt with on ordinary surgical lines and by sulphonamides or penicillin.

**Personal Prophylaxis.**—As infection is conveyed by drinking water from wells containing infected cyclops (water flea), which is the intermediate host of the worm, all water for drinking purposes should be strained through clean calico, such as villagers use for clothing. This removes the cyclops and is the simplest and most practical method of avoiding infection.\* No one should drink water from wells which are approached by steps, as this kind of well is the greatest source of infection. Wells should be closed and the water pumped from them.

**Onchocerca Volvulus.**—These worms cause small subcutaneous tumours in various parts of the body. Those about the head are often associated with ocular symptoms which may be very severe, leading finally to complete blindness. Consequently, in South America this worm has been known as the "Blinding Worm." Brumpt considers that the eye lesions may be due



to a distinct species, *O. cæcutiens*. The tumours may be removed under local anæsthesia, and removal of those on the head is said to be followed by improvement in the ocular lesions. Following excision a course of sodium antimonyl tartrate may be given. Doses of  $\frac{1}{2}$ ,  $1\frac{1}{2}$ , 2 gr. (0.03, 0.09, 0.12 gm.) respectively are given intravenously for the first three injections, 5 to 10 c.c. of sterile double-distilled water being used to dissolve the drug. A dose of 2 gr. (0.12 gm.) is then maintained for nine further injections. Proportionately smaller doses are given for children. Injections should be given very slowly. Recent observations suggest that antimony does not give such good results in this form of filarial infection as in others.

*Personal Prophylaxis.*—As the sand-fly is probably the vector of the infection, anti-sand-fly measures, as described under Leishmaniasis, should be instituted (see also p. 278). D.D.T. has been found to be particularly valuable in controlling the vector of this disabling infection.

## ANCYLOSTOMIASIS

(Hookworm)

**Specific Therapy.**—*Drugs Employed.*—Oil of chenopodium, tetrachlorethylene.

*Treatment.*—Combined treatment by tetrachlorethylene and oil of chenopodium gives better results than using the two drugs separately. After the preliminary treatment, as described on p. 270, the mixture (see p. 270) is administered in the morning, either in one or divided doses.

Glucose and carbohydrates should be included in the diet and 20 gr. (1.2 gm.) of calcium lactate given thrice daily for a few days previous to the administration of the mixture. A saline aperient should follow the mixture if there has been no movement of the bowels. The dose of tetrachlorethylene for children is 3 minims (0.18 c.c.) for each year of life. Chenopodium should not be repeated for at least a week.

It is important to warn the patient that *all* the dead worms may not be found in the first stool passed after the completion of the treatment, and that they may continue to appear for three days. Further, the eggs may be held up in folds of intestinal mucosa and can be found for at least a week after effective treatment has been completed. It is well to control treatment, where possible, by examination of the stools for ova by the direct centrifugal flotation method of Clayton Lane, which is very accurate.

*Toxic Signs.*—Tetrachlorethylene may cause damage to the liver and jaundice may occur. Chenopodium may cause depression of the respiratory centre.

For the treatment of *ancylostome dermatitis*, which usually affects the feet and is associated with the penetration of the larvæ through the skin, antiseptic foot-baths and a soothing ointment are useful. Three per cent. salicylic acid in ethyl alcohol has been recommended. This skin lesion is of considerable economic importance to planters with large labour forces in areas where ancylostomiasis is prevalent.

**Non-specific Therapy and Management.**—During convalescence from a heavy infection with ancylostomes the patient should be carefully supervised. A full dietary should be avoided as it is liable to cause enteritis. For

anæmia iron should be given as in secondary anæmia (see p. 470). If the anæmia is very marked it should be corrected before beginning anthelmintic treatment.

**Personal Prophylaxis.**—To prevent the larvæ from getting access to the skin, the universal use of boots in infected areas should be advised. All latrines should be kept in good condition. Salt spread over the soil in sufficient quantities to form brine will prevent the development of larvæ, and the washing of latrines with a 30 per cent. salt solution is also a valuable prophylactic measure.

## STRONGYLOIDIASIS

Infestation with *strongyloides stercoralis* is very prevalent in certain parts of the Far East and produces diarrhœa. Recently many persons have returned from active service suffering from this infestation.

**Specific Treatment.**—Gentian violet, as used in the treatment of threadworms (see below), has given good results. In refractory cases 25 c.c. of a one per cent. aqueous solution of the dye may be introduced directly into the duodenum by daily intubation for five days in the case of adults.

**Personal Prophylaxis.**—As in ancylostomiasis (see above).

## ENTEROBIASIS

(Threadworm)

**Specific Therapy.**—This infection, especially in adults, is often very difficult to treat. Diphenan—a carbamic acid ester of parahydroxydiphenyl methane—is given in doses of one to three tablets (0.5 gm.) daily for adults; for children over ten years the dose is the same and for younger children the dosage is proportionately smaller. The treatment should continue till twenty tablets have been taken. Enemata of quassia are used to expel the worms per rectum; the bowel is first washed out with a salt and water enema (one tablespoonful of salt to half a pint). Then 6 oz. of a 10 per cent. infusion of quassia are run slowly into the rectum and the foot of the bed raised. Medicinal gentian violet in enteric-coated tablets is useful. The dose for an adult is 1 gr. (0.06 gm.) three times a day before meals for eight to ten days. For children the daily total of 0.15 gr. (10 mg.) for each year of *apparent* age is recommended. Thus an undersized child receives less than a normal child of the same age. This daily total is given in divided doses three times a day. Serious organic disease of the kidneys or liver is a contraindication.

**General Management and Personal Prophylaxis.**—It is very important to prevent reinfection with ova; nails should be kept short and the hands washed constantly. The morning cup of tea before washing is a potent source of reinfestation. Close-fitting sleeping drawers and gloves of cotton should be worn at night. For pruritis ani the anus should be smeared at night-time with ung. hydrarg. ammon. (B.P.). By adopting these precautions reinfection with the ova will be prevented, as they are conveyed by contaminated hands and clothing, including bedclothes.

## ASCARIASIS

(Roundworm)

**Specific Therapy.**—Santonin is very commonly employed in the treatment of this infection in doses of 3 to 5 gr. (0.18 to 0.3 gm.) for an adult and  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) for a child. It may be given combined with 1 to 3 gr. (0.06 to 0.18 gm.) of calomel for three successive nights, followed by a saline purge of sodium sulphate six hours later. Santonin may cause visual troubles and make the urine yellow. The combination of tetrachlorethylene and oil of chenopodium in liquid paraffin, as described above, is also very useful as an anthelmintic in this condition. Lastly, hexylresorcinol has been found to be effective: The dosage varies from one pill (0.2 gm.) for children under three years, to five pills (1.0 gm.) for children over ten and for adults. A preliminary saline purge is given in the morning—no food having been taken since the previous evening—and, after the bowels have acted, the pills are given with a large draught of water. The patient should be warned that the dead worms may not appear in the stools for two or even three days after the completion of the treatment.

In some cases very large collections of worms may cause acute intestinal obstruction and surgical treatment may be necessary.

**Personal Prophylaxis.**—In areas where this infection is common, uncooked vegetables and other raw food material should be avoided.

## TRICHURIS TRICHIURA

(Whipworm)

Fortunately this worm does not give rise to serious pathological lesions, as it is very difficult to dislodge by any known anthelmintic treatment. A combination of tetrachlorethylene and oil of chenopodium may be administered as described on p. 270. Faust recommends that 8 to 10 oz. of a 1 : 1,000 solution of hexylresorcinol be introduced as a high enema and retained for fifteen to twenty minutes.

**Personal Prophylaxis** is the same as in ascariasis (*vide supra*).

## TRICHINOSIS

Man is an accidental definitive host of the worm *Trichinella spiralis* and becomes infested by eating the encysted larval trichinella in the muscles of the pig. In the human intestine adult worms develop from the larval forms with astonishing rapidity, and in as short a period as forty-eight hours after ingestion male and female mature worms can be found. After a further twenty-four hours embryos appear in the uterus of the fertilized female worm. The living embryos are voided into the lumen of the intestine. Travelling independently, via lymphatic and to some extent venous channels, they reach various striated muscles, diaphragm, intercostal, laryngeal, etc., where they become encysted.

The severity of the symptoms is proportionate to the number of larvæ ingested. In a number of cases no symptoms are produced at all and the infection is only detected after death. Hence it is important to distinguish

trichinosis as a disease and the presence in man of trichinella larvæ unaccompanied by apparent illness. The symptoms may be divided into acute and chronic, the former being associated with the presence of the adult worms in the intestine and during migration. At this stage the infection may be wrongly diagnosed as ptomaine poisoning, cholera or typhoid. In the stage of encystment the symptoms are more chronic and simulate rheumatism.

**Specific Therapy.**—The parasite can be attacked by anthelmintics only during the short period the adult worms are in the intestine. Hence the importance of early and accurate diagnosis. The drugs mentioned in the treatment of ancylostomiasis (p. 274) are applicable in this infection, particularly tetrachlorethylene, which has given promising results in the early treatment of the infection. Treatment after encystment is purely symptomatic.

**Personal Prophylaxis.**—Control must be along two lines, *viz.*, the adequate cooking of all pork and the elimination of the sources of infection of swine.

## INSECTICIDES, REPELLENTS AND ACARICIDES

### INSECTICIDES

#### D.D.T.

#### (*Dichlor-Diphenyl-Trichlorethane*)

The insecticidal powers of D.D.T. were discovered by Müller of the Swiss firm of J. R. Geigy, and patents date from March 1940. It has won a great reputation in military hygiene.<sup>†</sup> Although much investigation is still required to elucidate its potentialities, yet there can be little doubt that, following its wide use, a great reduction of disease-carrying insects has occurred and the tropical diseases which they transmit have been much more effectively controlled—a matter of first-class importance, since the mortality caused by insect vectors is on a gigantic scale and vast sums of money have been spent in attempts to destroy biting insects and in connection with the illnesses they cause; malaria alone accounts for about three million deaths annually.

D.D.T. is a white crystalline powder with a pleasant smell. It is non-volatile at ordinary temperatures, and is soluble in most organic solvents, though more soluble in crude mineral oil than in refined oil. It is stable in the presence of light, water vapour and boiling, and is without effect on metals, fabrics, leather and dyestuffs.

D.D.T. is employed as a solution in an organic solvent, as an emulsion dissolved in a solvent and then emulsified in water, or as a dust. These preparations are listed below.

**Toxic Effects.**—Lethal doses of D.D.T. for animals vary from 150-175 mg. per kilo of body-weight. Such doses, however, are very much higher than will ever need to be used in practice. It is unlikely to cause dermatitis even when dissolved in solvents. Taken by the mouth the dissolved D.D.T. is much more toxic than the solid form as the latter is not absorbed. Used as an insecticide D.D.T. is quite safe for mammals.

**Applications.—Mosquitoes.**—There is a great field for D.D.T. in the destruction of adult mosquitoes, as methods hitherto employed have not always been satisfactory or practical. The inside of dwellings, ships, etc., is sprayed with 5 per cent. D.D.T. in kerosene (Neocid spray) at the rate of one quart per 1,000 feet (about 50 mg. per square foot). One spraying reduces the number of mosquitoes to a very low level, and is effective for from two to three months. The spraying may be done by a pneumatic hand-sprayer with a capacity of two gallons. Fine atomization is undesirable and uneconomical. An extension of the use of D.D.T. is a 2 per cent. incorporation in whitewash, distemper and certain kinds of paint (not oil paint) used in dwellings, etc., which would be lethal to adult mosquitoes for two to four months after application. This outstanding "persistence effect" of D.D.T. is notable, and is a great advance on all insecticides hitherto used. Further, D.D.T. does not act as a repellent to mosquitoes, which was the great disadvantage of pyrethrum, as the latter caused the mosquitoes to fly from the room after spraying and thus prevented them from being killed.

D.D.T. in diesel oil is also very effective in destroying larvæ when sprayed on collections of water (0.10 c.c. per square yard) and the effect lasts for four days. D.D.T. may thus be the ideal prophylactic against malaria and may have a major effect on the disease in villages which are hardly touched by existing methods. Large areas can be treated by spraying D.D.T. from aeroplanes.

D.D.T. may play a very significant part in the prophylaxis of yellow fever. The spraying of the inside of planes with D.D.T. will destroy all adult *Aedes*; further, the present necessity of spraying the plane whenever it lands in certain parts of the world will be obviated.

**Lice, Flies and Fleas.**—Wide use was made of D.D.T. in the control of epidemic typhus in Naples in 1944. Insecticides hitherto used against the body louse (transmitter of epidemic typhus) failed because the effects were evanescent; further, the procedures were cumbersome, awkward and time-consuming, involving disrobing, and the dusting of garments by hand. In contrast, D.D.T. was applied directly by a compressed gun which blew it as a 10 per cent. dust up trousers and skirts, down sleeves, into collars, tucks and folds—wherever the lice might cling. This system of rapid dusting without disrobing enabled as many as 66,000 persons to be dealt with daily. More than 1,300,000 were treated in January 1944 alone. If well dusted, D.D.T. will protect the body against lice for four to five weeks. The epidemic in Naples, which might have caused thousands of deaths, thus collapsed with astonishing rapidity. As a measure against the body louse an even simpler procedure is to impregnate the garments by immersing them in a solution of Neocitex (see below). Thereafter they become insecticidal and remain capable of killing lice for some weeks even if the garments have been washed several times in hot water and soap.

Neocid dust (see below) applied to rat runways and burrows by a foot-pump duster is valuable as a prophylactic against plague and flea typhus.

The methods described in detail above can be used for the prevention of a variety of other insect-borne diseases, as for example, relapsing fever, sand-fly fever, kala-azar, tropical sore, dengue fever, filariasis, trypanosomiasis, plague, trench fever and flea typhus. Further, pests such as bed bugs, cockroaches and particularly house flies (important in the causation

of cholera, dysentery, enteric, smallpox and trachoma) are susceptible to the insecticidal powers of D.D.T. A 5 per cent. solution of D.D.T. in kerosene (1 quart per 300 square feet) is sprayed through a coarse nozzle, sufficient spray being used to give the surface sprayed a wet appearance but insufficient to cause the liquid to run off.

For head lice and crab lice the dusts used for the prevention of typhus are particularly effective.

The following preparations of D.D.T. for use as an insecticide are the products of Geigy, Manchester:—

- (1) Neocid Dust: 5 per cent. D.D.T. in inert powder.
- (2) Guesarol M.: Neocid Dust, with the addition of materials known as wetters and stickers, used for spraying by suspending in water.
- (3) Neocid Spray: 3 per cent. D.D.T. in kerosene.
- (4) Neocid M.R. Solution: A solution of D.D.T. with resin in a suitable solvent, used for spraying glazed brickwork or painted surfaces and leaving a colourless film.
- (5) Neocitex: 15 per cent. D.D.T. diluted with water and used as an emulsion for the treatment of fabrics, sheets, shirts, etc.
- (6) Neocid C.M. Emulsion: 2.5 per cent. D.D.T. for the treatment of head lice.

#### OTHER INSECTICIDES

**Gammexane** (I.C.I.).—This is a gamma isomer of benzene hexachloride which has similar insecticidal properties to D.D.T. In addition it has been shown recently to be lethal to scorpions, which are a serious menace to life and health in certain parts of the tropics. A talc powder containing 1 per cent. gammexane dusted in a room paralyses scorpions in from 30 to 60 minutes.

**Rothane** (Dichloro-Diphenyl-Dichlorethane) and **Lethane** (Beta-Butoxy-Thiocyano-Diethyl-Ethane) have given promising results recently. The latter is also a repellent (see below).

**Pyrethrum** and **Derris** have been largely replaced by D.D.T. or are only used in combination with it.

#### INSECT REPELLENTS

**D.M.P.** (Dimethyl phthalate).—This is now pre-eminent as an insect repellent and is included in the medical supplies of merchant ships to be used as a mosquito repellent when the ship enters malarious areas. After sunset a few drops are placed in the hand and applied to the exposed parts of the body, avoiding the eyes and the areas round the mouth. The effect lasts for about two or three hours, after which the application may have to be repeated. Veils, gloves, socks, etc., made of strong  $\frac{3}{8}$ -in. fishing net can be impregnated with D.M.P. and worn next the skin with garments covering them. This gives a high degree of protection and re-impregnation may only be required once a week. Impregnation of wide-mesh mosquito curtains is a valuable protection against sand-flies and small anophelines; such curtains are also more comfortable for use in the tropics than untreated curtains of fine mesh. Since D.M.P. is a solvent of plastics, paint and lacquer, it should not be smeared on such articles or on spectacles, watches and fountain pens.

**Lethane** (384).—50 per cent. in light oil sprayed on thin cotton garments is a useful repellent and has no action on plastics. It is unsuitable for direct application to the skin.

**Indalone** (2.2 Dimethyl-2-Carbobutoxy-7-Pyrone) has been found useful as a repellent of tsetse flies used in the following formula: Indalone 2 parts, D.M.P. 3 parts, and Rutger 612 (an American repellent) 2 parts.

**D.B.P.** (Dibutyl phthalate).—**Benzyl Benzoate**. See below.

### ACARICIDES

Mites of the *Trombicula* family are vectors of the very serious and widely distributed "scrub typhus" infection and are also the cause of the troublesome scrub itch and the newly recognized rickettsiapox, which strongly resembles chickenpox. The following are useful preparations in the control of such mites and give considerable protection to those who have to enter mite-infested areas if they are used intelligently. Equal parts of *benzyl benzoate* and *D.B.P.* are smeared on clothing or sprinkled on to it with a shaker bottle. This mixture gives good protection both as a repellent and as an acaricide and withstands laundering. Benzyl benzoate is obtainable as a 50 per cent. stable emulsion (B. W. & Co.). It is miscible in all proportions with water and does not stain clothing. It has also the important property of repelling the cercariæ of schistosomes, and by the use of gloves and stockings impregnated with it, the hazard of invasion of the skin by the cercariæ can be avoided and the serious condition of schistosomiasis prevented.

E. D. W. GREIG.

# SOME COMMON DISORDERS IN INFANCY AND EARLY CHILDHOOD

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## INTRODUCTION

**NURSING.**—The majority of diseases met with in infancy and early childhood are acute. Infections are more common and fraught with more serious consequences than in adults. Except where specific remedies are known, treatment is necessarily restricted to measures which help to tide the patient over the acute period. The recuperative powers of children, however, are great, and once an acute infection is overcome, convalescence is as a rule rapid. The most important therapeutic measures are nursing, the administration of a suitable diet and the giving of a plentiful supply of fluid. Drug treatment plays a minor part, though stimulants and sedatives may be of the greatest value on occasions.

The sick infant should, where possible, have a room to himself and on no account should a bed or cot be shared. The temperature of the room is best kept between 60° and 65° F. The child's clothing should be loose and comfortable. Harsh woollens next the skin are often irritating. After the umbilical stump is healed a binder is no longer required; it impedes respiratory movement and is also a source of skin irritation. Great care should be taken to prevent skin infection; a sweat rash which would not be more than a source of irritation in the adult may lead to widespread and serious skin infection in the infant. Frequently it is difficult to prevent a child from scratching or picking at an infected area on the skin. To prevent this the arms should be splinted so that the elbows cannot be flexed. The best method of doing this is to bandage strips of cardboard to the arms, extending from the axilla to the hand. The infant should be bathed in the morning and sponged at night. The buttocks require special attention and should be carefully sponged each time the napkins are changed. If there are any signs of irritation a bland ointment such as zinc and castor oil may be applied freely. Tepid sponging for skin temperatures above 102.5° F. is valuable and often promotes sleep in addition to reducing the fever. The sick infant should not be allowed to lie in one position for too long, and in acute respiratory disease he should be propped up with pillows.

**Diet.**—A discussion on infant feeding is outside the scope of this work, but we would emphasize the importance of feeding the infant on uncontaminated milk. This can best be ensured by breast feeding, but, failing that, dried-milk preparations are much safer than even the highest grade of liquid cow's milk. The dried powder is unlikely to become grossly contaminated, and if each feed is made up immediately before it is given, there is little chance of pathogenic organisms gaining access. Liquid milk, even though sterilized by boiling or pasteurization, may readily become re-infected. As older children are less liable to gastro-intestinal upset, ordinary cow's milk may legitimately be used in their diet, but the milk should



always be heat sterilized. Generally speaking, in febrile conditions the food intake should be diminished as regards fat, but an adequate supply of carbohydrate in the form of cane sugar (or glucose) is to be recommended. These principles can be put into practice by using one of the half-cream dried-milk preparations or by diluting liquid milk to half strength and adding sugar, while maintaining or even increasing the total fluid intake. Beef-tea, soup and cereals do more harm than good in acute illness. The first two have very little food value and limit the amount of fluid that can be taken as milk, while cereals are apt to upset digestion.

It is of the utmost importance to ensure that the ill infant receives an ample supply of fluid. Unlike the adult he cannot ask for a drink, so water must be offered at frequent intervals. There is no condition, except perhaps gastric or bowel perforation, in which unlimited fluid should not be given. It is not unusual for a well-nourished infant weighing, say, 12 lb. to lose 8 oz. (*i.e.*, one-twenty-fourth of his weight) in the first twenty-four hours of an acute diarrhoeal disease. This loss of weight is almost entirely accounted for by loss of fluid from the blood and tissues. So prone is the young child to become dehydrated and so evil are the consequences that it is frequently necessary to give fluid by routes other than by the mouth. It is best given as plasma or in the form of half-normal saline solution with or without the addition of glucose in a concentration of 10 per cent.

**Drugs.**—The administration of drugs is often difficult. It is better to give them in solution rather than as powders. It is impossible to give pills unless they are ground into powder and mixed with water. The infant's sense of taste is not well developed, and he will readily take medicine highly unpalatable to the adult. The dosage must be modified according to age, the usual formula being  $\text{adult dose} \times \frac{\text{age}}{\text{age}+12}$ . Using such a formula there

is little if any likelihood of overdosage and there are many drugs which may be given in much larger doses than the use of the formula would suggest—*e.g.*, chloral hydrate, belladonna and its active principle, atropine, and calcium or ammonium chloride. Preparations containing strychnine as well as opium and its derivative, morphine, must be given with caution. The most useful sedative for young children is chloral hydrate. It is particularly safe and has no cumulative effects. Acetyl-salicylic acid will also be found efficacious. Where a stronger sedative is required, *e.g.*, in status epilepticus, paraldehyde given in saline or olive oil per rectum in doses up to one drachm per stone of body-weight will be found effective. The use of strong cathartics is seldom if ever necessary. Drastic purgatives are dangerous on account of the serious loss of fluid entailed. The brisk purge commonly given to an adult at the onset of an acute infection is neither necessary nor advisable in the infant. The most useful laxatives are fluid magnesia, syrup of figs and paraffin preparations; frequent and long-continued use of mercurials such as mercury and chalk cannot be recommended.

A suitable method of giving medicine to an infant is to place him in the semi-erect position with the arms enclosed in a blanket or shawl wrapped round the body. The mouth can be opened by gentle pressure on the cheeks with the thumb and forefinger of the left hand and the medicine poured from a teaspoon held in the right hand well into the back of the mouth. In order to get him to swallow, it is sometimes necessary to compress the nostrils for a few seconds.

### SPECIAL METHODS OF FEEDING

Sometimes on account of grave debility or deformity of the lips and mouth (hare-lip and cleft palate) the infant is unable to suck either the breast or the bottle. In those circumstances special methods must be employed. The commonest of these is spoon-feeding. This is often invaluable although time-consuming. Another method is to give the food by a pipette to which a small piece of rubber tubing has been attached. The food can be introduced drop by drop into the back of the throat. For the child too weak to swallow or for one whose swallowing reflex is in abeyance, resort must be had to feeding by stomach tube. This is known as gavage, and can only be adopted when skilled nursing is available. The child must be wrapped in a blanket enclosing his arms and laid on his side across the nurse's knees. The apparatus required comprises a glass funnel connected by rubber tubing and a short glass connecting piece to a small stomach tube (No. 8 to 10, English). The tube is lubricated with glycerin and inserted through the mouth into the stomach. A rough estimate of the length of tube to be passed in order to reach the stomach may be obtained by measuring the distance from the mouth to the xiphisternum. The tube may be marked by a thread tied round it at the appropriate distance from its point. After the tube has been inserted any residue of food lying in the stomach is withdrawn by siphonage and the food is then run into the stomach. The tube should be withdrawn slowly and compressed between the finger and thumb to prevent reflux into the larynx.

A similar apparatus may be employed for gastric lavage. The fluids used for this are normal saline solution or a solution of bicarbonate of soda, a teaspoonful to the pint of water.

### SPECIAL METHODS OF GIVING FLUID

Extra fluid may be given to infants by the rectum, although in diarrhoeal conditions this is useless as it cannot be retained and may act as an irritant. Fluid may also be given parenterally, *i.e.*, by routes other than the alimentary tract, such as into the subcutaneous tissues, the peritoneal cavity or a vein. Administration of fluid by injection into the bone marrow has been advocated. In young children the sternal marrow is so scanty that this route is not practicable, but the tibial marrow may be used instead; special needles are made for this by Allen & Hanbury. In our opinion the grave consequences that occur if infection should arise make this method undesirable. For parenteral use, normal saline with or without the addition of 5 per cent. glucose is most frequently used. Plasma in full strength or diluted with an equal amount of glucose saline is probably better than saline alone. The presence of the plasma assists in the retention of fluid in the circulation. Recently it has been suggested that potassium chloride is required to make good the loss of potassium in the stools, but it must be used with caution as an accumulation of potassium in the blood will cause intoxication with peripheral circulatory failure and collapse. Ringer's, Locke's and Hartmann's solutions, as well as the one recently recommended by Darrow, all contain potassium. If large quantities of saline have to be given parenterally it is advisable to give it in half normal strength, as in young children accumulation of chlorides in the tissues readily occurs.

**Rectal Administration.**—A rubber rectal tube (size No. 10) to which a funnel is attached is, after lubrication, gently inserted into the rectum to a distance of 2 to 4 in. (5 to 10 cm.) and the bowel washed out; after the rectum has been emptied, 2 to 4 oz. (60 to 120 c.c.) of warm normal saline with glucose (5 or 10 per cent.) are run in slowly and the tube withdrawn. The buttocks should be held together for a few minutes after withdrawal of the tube. This procedure may be repeated after an interval of four hours. Young infants cannot as a rule retain more than 2 oz. (60 c.c.) at a time. When there is diarrhoea or rectal irritation this method of giving fluid is impracticable.

**Subcutaneous Route.**—This is the simplest of the three methods of giving fluid parenterally. Two needles connected by a glass Y-piece with a rubber tube leading from a funnel may be used. They are inserted into the subcutaneous tissue below the breasts or in the axillæ. The fluid is run in by gravity, and if given slowly by the continuous drip method little or no pain is caused and as much as 500 c.c. can be given in twenty-four hours.

**Intraperitoneal Route.**—This method has gained considerable popularity in recent years, and properly carried out is devoid of danger. Any suspicion of acute abdominal disease of a surgical nature or tuberculous peritonitis must obviously be regarded as a contraindication. Having made sure that the bladder is empty, a needle having a short bevel with a bore of 1.2 mm. and a length of 30 mm. is inserted into the peritoneal cavity at a point  $\frac{1}{4}$  in. below and to one side of the umbilicus. Strict aseptic precautions must be observed. The fluid at a temperature of 103° F. in the reservoir is run in by gravity and 100 to 200 c.c. can be given, depending on the age of the patient and the degree of dehydration. It is recommended that glucose solution be not used because of the increased risk of infection.

**Intravenous Route.**—This is the most direct, rapid and effective method of giving fluid. The principles involved are similar to those obtaining in the adult. Veins in infants are much smaller, however, and it is frequently necessary to cut down and expose a vein under local anæsthesia and to tie in a small Bateman's cannula. For this the internal saphenous vein, as it crosses the internal malleolus, will be found suitable. Employing very fine needles (0.8 mm. bore), scalp veins can often be utilized. The fluid should be given slowly either by injection from a syringe or preferably by continuous drip. In the latter case it is advisable, before commencing the operation, to immobilize the limb with a splint. About 120 c.c. of fluid per kilo of body-weight may be given in 24 hours. When there is severe dehydration or anæmia, the intravenous drip is often a life-saving measure.

In infants in whom the anterior fontanelle is still patent, fluid may be administered through the superior longitudinal sinus. Although this route was popular in the past, it is not without danger from escape of the injected fluid into the brain and meninges, and should only be used in emergencies and by those experienced in the technique. Blood may, however, be removed from the longitudinal sinus when several centimetres are required for a Wassermann test or blood culture and is in our experience free from risk. The method is as follows: the child should have his arms pinioned by being firmly wrapped in a blanket or shawl. He should be placed with his head resting on a hard pillow at the end of the table. His head should

be firmly held with a hand on each side of the face. The operator should be seated at the end of the table. The hair is shaved from the region of the fontanelle and the skin sterilized. A short bevelled needle with syringe attached is then inserted through the scalp at a point immediately anterior to the posterior angle of the fontanelle in a downward and backward direction, the needle pointing towards the occipital protuberance. The sinus is reached at a depth of about 0.5 cm. As the needle is being inserted, negative pressure can be created in the syringe by traction on the piston, and when the sinus is entered a jet of blood will be drawn into the syringe. If fluid is to be administered, the needle is connected by tubing to a glass funnel and the fluid allowed to run by gravity. On removal of the needle, firm pressure with a sterile gauze swab should be made over the needle puncture for one or two minutes.

## NEO-NATAL CONDITIONS

**Prematurity.**—Any infant whose birth weight is 2.5 kilo ( $5\frac{1}{2}$  lb.) or under should be regarded as premature. As this condition represents one of the four principal causes of neo-natal death, the treatment and care of these small infants is one of great importance and responsibility. Ideally, the best form of treatment is prevention, but, unfortunately, the cause of premature birth in at least half the cases is unknown. There is considerable evidence that an inadequate diet, especially during the last three months of pregnancy, increases the incidence of prematurity. Likewise, its incidence is highest among mothers who are of poor physique and who are living in conditions of poverty and squalor. The prevention of prematurity is therefore a national problem, linked up with the general health of the women of child-bearing age and their economic position. Under present conditions, good ante-natal care, using the term in its widest sense, is the most important factor in preventing the high mortality caused by premature birth.

The chance of survival in any given case depends on the weight of the infant and on the presence of disease or injury. With experienced nursing skill and attention to detail much can be done even for very small and weakly babies. The first essential is to prevent heat loss. A severe chilling, which is most likely to occur in the first few hours after birth, may alone be responsible for the infant's death. In all cases in which it is suspected that the infant will be small, special preparation should be made for his reception. A bassinet with the necessary blankets and hot-water bottles must be in readiness, and someone must be detailed to care for the infant as soon as he is born. If there is cyanosis, artificial respiration should not be attempted, but one must make sure that the air passages are not obstructed. They may be cleared by a mucus extractor—a small bottle with a two-way stopper fitted with two soft rubber tubes, one of which is inserted into the throat, the other is used to create negative pressure, either with the mouth or a rubber bulb; attempts to remove mucus by the finger wrapped in gauze are ineffective and dangerous. The infant should not be bathed; it is sufficient to cleanse the body rapidly with olive oil. Indeed, all bathing should be avoided until his temperature becomes stabilized and he is thriving. Tight clothing is contraindicated. He should not be "dressed" but wrapped in a jacket made of gamgee with a hood to cover the head

and fastened with tapes down the front. Instead of a napkin a square of gamgee placed under the buttocks should be used; it can be discarded when soiled and is less irritating to the skin than the napkin. Even the binder should be loosely applied lest it interfere with respiration. The blanket over him should be as light as is consistent with sufficient warmth and an extra blanket can be placed over the bassinet as further protection. He can be carried about in this way without loss of heat or undue disturbance. Hot-water bottles to supply the necessary warmth are usually required, but the greatest care must be taken to prevent burns. The electric blanket may also be recommended and is of special value in institutions; it should always be covered by some non-conducting material such as rubber; serious burns have occurred when this precaution has not been observed. It should be placed over, not under, the child and, if necessary, it may be supported by a cage. The infant should have a room to himself, with ample fresh warm air. The room should be kept at a temperature of 70° F. Elaborate or complicated incubators are only practicable in institutions and cannot be recommended for general use.

Every possible care should be taken to prevent infection. Skin abrasions if present should be treated twice daily with a 1 per cent. aqueous solution of gentian violet and left, preferably without dressings, exposed to air as much as is practicable. The point should be stressed that any person who is even suspected of having a cold should have for the time being no access to the infant. All utensils, bottles and teats used for feeding must be cleaned and boiled with meticulous care each time they are used.

The feeding of the infant is greatly simplified if breast milk is available, and every attempt must be made to procure this, if not from the mother, from a foster-mother. If it cannot be obtained, one of the half-cream dried milks (half-cream Cow & Gate, No. 1 Ostermilk, half-cream National Dried Milk) may be used. One to two ounces (30-60 ml.) of reconstituted dried milk to which has been added half a teaspoonful of cane sugar or dextro-maltose is a suitable feed to begin with.

If the infant is strong and breast milk is available, he should be put to the breast in the ordinary way; if he is too weak to suck, the milk must be exhausted, boiled and fed to him either by spoon or pipette. A valuable method is gavage. It has the great advantage of diminishing the time taken in feeding, thus allowing him more time to sleep. If he is fed by gavage a four-hourly interval will probably suffice; if by any other method, in the early stages at any rate, it is better to feed him three-hourly. Only in exceptional circumstances is it advisable to feed a premature infant more often.

Premature infants are prone to develop rickets and iron deficiency anæmia. It is important that steps be taken to prevent these nutritional defects. Because of their rapid growth it is now recognized that these infants require more vitamin D than full-term infants—about 1,400 I.U. daily instead of 800-1,000. In the winter time and in large industrial centres, this amount can with advantage be increased to 2,000 I.U. About the end of the first fortnight cod-liver oil in doses of half a teaspoonful night and morning should be given and the amount steadily increased to a minimum of one teaspoonful three times a day. Ordinary cod-liver oil contains at least 85 I.U. of vitamin D per gm. The cod-liver oil supplied by the Government is fortified with synthetic vitamin D so that one teaspoonful supplies

700 I.U. The B.P. calciferol solution, two or three drops (1,000-1,500 units), or any of the numerous proprietary preparations (adexolin, ostelin, radiostol, haliverol, etc.) in adequate doses is equally satisfactory. In using a concentrated preparation, measured in drops, it is well to instruct the mother to give it by spoon, not to put it into the feed. Iron may be given later, beginning about the tenth or twelfth week. A suitable formula is:—

R7	Ferr. Sulph.	.	.	.	.	gr. i (0.06 gm.)
	Cupr. Sulph.	.	.	.	.	gr. $\frac{1}{100}$ (0.6 mg.)
	Acid. Hypophosph. Dil.	.	.	.	.	M $\frac{1}{2}$ (0.03 c.c.)
	Dextros.	.	.	.	.	gr. xv (1 gm.)
	Aq.	.	.	.	.	ad fl. dr. i (4 c.c.)

Sig., fl. dr. i (4 c.c.) t.d.s.

It is important that ferrous sulphate be prescribed in this way to prevent oxidation. Iron and ammonium citrate gr. x (0.6 gm.) may be given in place of ferrous sulphate. There is good evidence to show that the hæmoglobin level will rise higher with the addition of copper than with iron alone. Certain of the dried milks (Hæmolac, Ferrolac) have iron added and under certain conditions will be found useful. After the fifth month, if a good mixed diet of iron-containing foods cannot be ensured, the iron mixture should be continued throughout the first year. The vitamin D preparation should be given throughout the first year and during the winter months for the next few years. Vitamin C may be given as orange juice, hip jelly or black currant purée, or in the form of ascorbic acid, in doses of 25 to 50 mg. daily.

**Inanition Fever.**—This condition is recognized by a sudden rise in temperature in an infant during the first week of life without there being any evidence of infection or cerebral trauma. It occurs at the period when the mother's milk is probably inadequate; hence the name. Actually the *causa causans* is lack of fluid, *i.e.*, dehydration. The child should be given 4 to 8 oz. (120 to 240 c.c.) of water or normal saline during the course of a few hours. This will cause the return of the temperature to normal: if it does not, the diagnosis should be reconsidered.

**Sepsis Neonatorum.**—This condition has greatly diminished in frequency. The infection usually gains entrance either through a skin abrasion or by the umbilicus. Prevention consists in guarding all abrasions of the skin from infection by suitable antiseptic measures and by the use of sterile dressings for the umbilical stump. The best antiseptics are a 1 per cent. aqueous solution of gentian violet, acriflavine (1 : 1,000) or surgical spirit. Iodine is unsuitable. If the infection becomes generalized, *i.e.*, septicæmic, the outlook is grave and no form of treatment is likely to be of any avail. If pemphigus appears the dead skin must be carefully cut away and the raw area treated with antiseptics. Treatment of this type of infection with sulphonamide preparations has proved disappointing, but penicillin by mouth in doses of 5,000 units per pound of body-weight a day has given promising results, especially in staphylococcal infections. Such patients must be isolated from other infants as this type of neo-natal sepsis is extremely contagious.

**Epidemic Diarrhoea of the Newborn.**—Within recent years, under this title, epidemics of diarrhoea occurring in newborn babies have been described both in this country and America. There is no doubt of the infectious nature of the condition, but so far no causal agent has been discovered. It

is only seen in institutions, and in dealing with such an outbreak the unit concerned should be closed and all contacts isolated. In treating the individual case, all feeds should be omitted for a period of twelve hours and one-quarter-strength normal saline given. Parenteral fluid (glucose saline with or without plasma) may be required at this stage if the condition of the infant requires it. After this period of initial starvation, half-ounce feeds of boiled breast milk or half-cream dried milk may be given every three or four hours. Each feed is increased in amount by half an ounce (15 c.c.) per day until the required amount is given. The fluid intake must be kept up during this time. If the mother has breast milk the baby should be allowed to feed at the breast as soon as possible. If artificially fed, sugar as dextro-maltose or cane sugar should be added cautiously. Drugs have little place in the treatment of this condition, but as penicillin by mouth is effective at this age, it is as well to give 5,000 to 10,000 units at the beginning of each feed. The sulphonamides, especially those poorly absorbed such as sulphaguanidine or succinylsulphathiazole, are recommended by some.

**Hæmorrhagic Disease of the Newborn (Melæna Neonatorum).**—The diagnosis of this condition rests on the recognition of the occurrence of bleeding in an infant in the first twelve days of life. Bleeding may be from the bowel (melæna), from the umbilical stump, into the skin or into any of the viscera or body cavities, such as the meningeal spaces or the pericardial sac. The condition is probably due to vitamin K deficiency, and it is claimed that it can be prevented by administering the vitamin to the mother immediately before or during labour. Its gravity and the response to treatment may be gauged by repeated hæmoglobin estimations. If life is to be saved it is essential that the condition be recognized early and active treatment instituted without delay.

Blood transfusion is by far the best form of treatment. Even infants who appear moribund may show dramatic recovery after transfusion. It is wise to cross-match the blood even if blood from a universal donor is employed. Fifteen to 30 c.c. per kilo body-weight can be given depending on the severity of the blood loss. In mild cases, or in those for which transfusion cannot be arranged, one of the analogues of vitamin K (Menaphthone, Kapon, Prokayvit) should be used. The vitamin can be injected intramuscularly in 1 c.c. (10 mg.) doses and repeated if necessary in four hours.

In view of the urgency for treatment, and when transfusion is impossible or vitamin K not available, whole blood should be injected subcutaneously. Ten to 20 c.c. of blood should be withdrawn from a healthy donor and immediately injected into the loose subcutaneous tissue between the scapulæ. The procedure is repeated in four hours. Grouping is not necessary. Blood-stained motions may continue to be passed after the bleeding has ceased, and some difficulty may be experienced in deciding whether further treatment is required. Hæmoglobin estimations will serve as a guide, but when in doubt treatment by one or other of the recognized methods should be continued. If there is extensive hæmorrhage into a vital organ no form of treatment is likely to be of any avail. Prevention may be achieved by giving the mother 10 mg. of one of the vitamin K analogues by the mouth at the onset of labour, but, as the incidence of this condition is about 1 in 800 births, the necessity of this as a routine may be questioned.

**Jaundice.**—Jaundice in the newborn is most frequently physiological. It is due to the destruction of erythrocytes in the first few days of life, during which time the hæmoglobin content of 140 per cent. at birth falls rapidly below 100 per cent. It is probably correct to say that 30 to 60 per cent. of all newborn infants are to some extent jaundiced. The general health is unaffected and there are no signs of biliary obstruction. No treatment of the condition is required.

**Biliary Atresia.**—True obstructive jaundice may arise from congenital malformation of the bile ducts. It is differentiated from icterus gravis by the absence of anæmia and of reticulocytosis. In the majority of cases the outlook is hopeless, although death may be delayed for several months or even years. In a few cases in which the gall-bladder has been proved to be present operative measures have been employed, occasionally with success.

**Sepsis**, where the infection is generalized, may produce jaundice from hepatic involvement or from hæmolysis. The outlook, of course, is grave, and the usual measures for dealing with septicæmia should be adopted. *Congenital syphilis* is often mentioned as a cause of jaundice, but its incidence is probably casual and not as great as formerly believed. The treatment is that of congenital syphilis.

**Erythroblastosis Fœtalis (Hæmolytic Disease of the Newborn).**—The primary fault in this condition is an acute hæmolysis of the infant's red cells. Although it is likely there are other factors, one of the most common is the presence in a rhesus-positive infant's blood of the recently discovered rhesus antibodies derived via the placenta from the P<sup>h</sup>-negative mother's blood (see p. 937). The presence of these antibodies leads to the destruction of the infant's red cells.

In its earliest and most acute form (*hydrops fœtalis*) the infant is born dead. In the less acute forms the condition is recognized either as *icterus gravis* (biliary obstruction) or as a slightly milder form, congenital hæmolytic anæmia. It is possible that some of the cases of physiological icterus are examples of this disease in a mild form and as such require no special treatment. In all cases where the hæmoglobin falls below 80 per cent., treatment by transfusion should be given. If jaundice is severe the outlook is grave and transfusion will not be found helpful in restoring liver function, although in practice it may be unwise to withhold this form of therapy. It is essential that blood from an Rh-negative donor (not the mother), who has not had a previous transfusion of Rh-positive blood, should be used. All maternity and children's hospitals should have a store of Rh-negative blood of known ABO group or a list of suitable donors who are available at short notice. The cessation of the hæmolytic process can be gauged by hæmoglobin estimation and reticulocyte counts. Large transfusions, 15 to 25 c.c. per pound of body-weight, given by the drip method if possible, are required and they may have to be repeated.

**Birth Injuries.**—Birth injuries are extremely common, and, when involving the central nervous system, often serious. Their early recognition is most important if the best results from treatment are to be obtained.

A *cephalhæmatoma* which consists of an effusion of blood beneath the periosteum of one of the flat bones of the skull is often a cause of considerable apprehension to the mother. Any attempt to remove the blood clot



by aspiration or by incision is to be condemned. The risk of infection is too great. If left untreated such swellings disappear in two or three months and leave no traces. The possibility of a cephalæmatoma becoming infected even although not interfered with does, however, exist, and in such circumstances it should be dealt with surgically.

The commonest sites of *fracture* in the newborn are clavicle, femur and humerus. They are not, curiously enough, of the "greenstick" variety but complete. Displacement may be great, but in otherwise healthy infants healing readily occurs without deformity. Fractures of the clavicle require no special treatment; indeed probably only a small percentage of them are recognized. For the fractured femur a band of adhesive tape, 2½ in. wide, is bound around the site of the fracture and the infant suspended by the legs from a light bar placed across the upper rail of the cot so that the buttocks are just free of the mattress. The weight of the child is sufficient to overcome any slight muscle spasm and produce satisfactory alignment. Another method is to flex the thigh on the abdomen and fix it there with adhesive plaster. The advantage of this method is that the child can be removed from the cot in order to be breast-fed or cleansed. The limb should be kept fixed by one or other of these methods for a fortnight or three weeks, following which free movement can be permitted. The fractured humerus should also be bound up with a band of adhesive tape and the arm bandaged across the chest for a fortnight. It has been claimed that without any immobilization such fractures heal well and that good alignment is obtained, but the infant will be made more comfortable if some simple form of fixation is used. Before fixing fractures of long bones the skin should be bathed with spirit and thoroughly powdered, special attention being paid to axilla, antecubital area and the groin.

Fractures of the skull are not common, but what is seen not infrequently is a gutter or funnel-shaped depression of the skull with no actual fracture, usually situated on the lateral aspect of the skull well forward. There have been many suggestions for dealing with such conditions surgically, but in the absence of signs of cerebral irritation they are much better left alone. The deformity, unless it is very severe, will disappear during the first year and the normal contour of the skull be restored.

*Cerebral birth trauma* is extremely common though the diagnosis is often not apparent. It occurs most frequently in premature infants and is often associated with asphyxia. The trauma may result in cerebral hæmorrhage, œdema of cerebral tissues or rupture of the meninges with hæmorrhage. Among the manifestations of the condition may be mentioned convulsions, attacks of cyanosis, tense or bulging anterior fontanelle, inability to suck, shrill piercing cry and fever. Subtentorial lesions are more likely to result in death than those above the tentorium. The patients often present the picture of asphyxia pallida (shock). Rest and warmth in a quiet darkened room with a minimum of disturbance constitute an important part of the treatment. If there are signs of increased intracranial pressure, such as fullness of the anterior fontanelle or undue drowsiness, lumbar puncture should be performed to relieve the pressure and should be repeated if necessary. The injection of 1 to 2 oz. (30 to 60 c.c.) of 10 per cent. saline solution into the rectum, repeated four-hourly, has been advocated as a means of lowering intracranial pressure. Its value, however, is doubtful. Chloral hydrate should be used freely if the infant is twitching or if he is

restless. One or two grains (0.06 or 0.12 gm.) three or four-hourly will be required; the dose must be increased until rest is obtained. If the signs and symptoms point to hæmorrhage over the cerebral cortex, surgical intervention may be considered. This is an extreme procedure, however, and the greatest difficulty is experienced in deciding on the case which offers a reasonable chance of success, especially as the lesions are so often multiple.

Certain authorities hold that cerebral hæmorrhage is often a result not of trauma but of hæmorrhagic disease of the newborn, and recommend that cerebral hæmorrhage in the absence of a history of birth injury, and coming on several days after birth, should be treated by subcutaneous injections of whole blood or of vitamin K as in hæmorrhagic disease.

*The seventh cranial nerve* is often injured in newborn infants. As a rule this is the result of pressure at the stylomastoid foramen; no treatment is required and certainly not electrical stimulation.

*Brachial paralysis* (Erb-Duchenne) resulting from injury to the brachial plexus and producing a flaccid paralysis of one or other arm should be treated as soon as it is recognized. The arm should be raised above the level of the shoulder with the forearm flexed at the elbow to a right angle and held there by pinning the sleeve to the pillow. In many mild cases that is all that is required and, after a fortnight or three weeks of such treatment, full power may have been restored to the arm. Care must be taken during this time that the nerve trunks and affected muscles are not allowed to become stretched. During the bath, for instance, the affected arm must be carefully supported. In more severe cases some form of splint holding the limb in a position of abduction and external rotation at the shoulder and flexion and supination at the elbow will be required. The best material for a splint of this nature is vulcanized fibre. It should be remembered that at this age growth is very rapid, and too elaborate a splint is not advisable, as the baby will soon outgrow it. The further treatment of this condition belongs to the field of orthopædic surgery.

## DISEASES OF THE DIGESTIVE SYSTEM

Disease of the digestive system is probably the commonest cause of illness in infancy and early childhood. In some of the acute conditions treatment must be carried out with promptitude if life is to be saved, while in certain of the more chronic disturbances a systematized plan of treatment which may have to be continued for a prolonged period has to be instituted. Hard-and-fast rules cannot be laid down for the treatment of individual cases, but there are certain general principles which should be borne in mind.

1. Breast feeding must be regarded as infinitely superior to artificial feeding. It may be taken for granted that a mother's milk is the most suitable food for the infant, and the practice of taking babies off the breast because of "upsets" is to be deprecated. It is seldom that mother's milk is so defective in quality as to justify weaning.

2. It is in the summer and autumn months that gastro-intestinal disturbance is most likely to occur. For this reason a correct system of feeding hygiene should be most carefully observed during this period.

3. Parenteral infection is a common cause of gastro-intestinal upset. In all cases of gastro-intestinal disturbance extra-alimentary foci of infection should be sought for and dealt with.

4. In the chronic affections careful investigation of the previous feeding history and thorough physical examination are of great importance in affording a guide to treatment. In many cases cure may be effected merely by correcting errors in the diet, while in others careful examination may reveal unsuspected deformities or foci of infection which are the cause of the gastro-intestinal disturbance.

### STOMATITIS

Injury to the mucous membrane is the most usual cause of inflammatory conditions of the mouth and pharynx. The mouth of the infant requires no cleaning and attempts to do so may, by injury to the mucous membrane, give rise to stomatitis. Other causes are unclean rubber teats and comforters. In order to avoid mouth infection a mother should be warned against making any attempt to clean her baby's mouth after feeding, and in the case of the artificially fed infant the importance of sterilizing everything coming into contact with the mouth should be emphasized.

**Parasitic Stomatitis (Thrush).**—The condition is speedily remedied by painting the affected areas with 1 per cent. gentian violet in aqueous solution thrice daily for a period of three to four days. Such preparations as glycerin and borax are ineffectual. The condition is most frequently seen in marasmic infants, and in addition to local treatment every effort should be made to improve the general condition.

**Aphthous Stomatitis.**—The child should be given potassium chlorate by the mouth at four-hourly intervals in doses of 2 to 7½ gr. (0.12 to 0.45 gm.) according to the age, and the ulcers should be touched with a 1 per cent. solution of silver nitrate. *Ulcerative stomatitis* requires more energetic treatment on similar lines. In addition, a solution containing equal parts of liquor arsenicals and tincture of ipecacuanha in an equal amount of glycerin may be painted on the gums and buccal mucous membrane with a camel's-hair brush. It is now recognized that this condition responds well to penicillin used locally. A solution containing 1,000 units to the c.c. of saline should be applied to the mucous membranes four-hourly. Improvement is rapid and only in specially serious cases is systemic administration required.

**Bednar's Ulcers.**—Sometimes ulceration of the pillars of the fauces and soft palate occurs in young infants. These ulcers are usually caused by misguided efforts to clear secretion from the mouth and pharynx of the newborn infant. They should be painted with a 1 per cent. solution of silver nitrate.

**Dental Caries.**—It is widely held that dental caries is caused by the acids produced from carbohydrate fermentation in the spaces in and around teeth, and that this is specially liable to occur in poorly calcified teeth. The indications, therefore, are to limit the consumption of sticky sweets (toffee, chocolate), to encourage a diet of hard and fibrous substances, *e.g.*, rusk, toast, fruits such as apple, and to ensure an ample supply of vitamin D and milk. A soft brush should be used to clean the teeth, care being taken not to injure the gums. No food should be given after the evening dental toilet.

### VOMITING

The treatment of vomiting depends on its cause. Mothers frequently seek advice because the baby brings up mouthfuls of milk after each feeding. In many cases this is not of serious significance, and if weight is being gained satisfactorily it may be disregarded. Sometimes, however, there is considerable loss of food and the infant does not thrive. In these cases there is probably some error in feeding technique. It may be that the child is placed flat on his back immediately after taking his feed and, in his endeavours to eructate ingested air, brings up mouthfuls of food. To prevent this he should be held in the semi-erect position for some minutes after he has finished his feed. In other cases irregular feeding and unsuitable food are responsible for vomiting. Here the treatment consists in correcting the defects in the feeding regimen and the diet.

**Rumination.**—Some infants acquire the habit of purposefully regurgitating ingested foods. When this habit has become well established it is difficult to correct and may lead to severe inanition. Various mechanical devices, such as pledgets of wool to plug the nostrils or gags which prevent the mouth from being opened, have been advocated, but they rarely meet with success. Probably the best results are obtained by getting the mother or nurse to occupy the child's attention after each feeding till he falls asleep. Thickened feeds, being more difficult to regurgitate, are also helpful. Any of the farinaceous foods, such as oat flour or Sister Laura's Food, may be used for this purpose.

**Œsophageal Stenosis and Cardiospasm.**—The symptoms of stenosis and cardiospasm which usually manifest themselves when the child commences to take solid food may be treated by dilatation with gum elastic Œsophageal bougies. On the first occasion this should be done under direct observation through an endoscope in order to guard against the disaster of perforating an ulcer situated above the site of the obstruction. Dilatation may have to be carried out daily at first and then, as improvement occurs, at gradually increasing intervals.

**Mechanical Obstruction at the Pylorus.**—This is a common cause of intractable vomiting in young infants. The obstruction may be due to spasm of the pyloric sphincter or to spasm combined with hypertrophy of the muscle (hypertrophic pyloric stenosis).

In *pylorospasm* treatment should be carried out on purely medical lines. Gastric lavage with normal saline solution should be used daily till the vomiting becomes less frequent. Whenever possible breast feeding should be employed. Failing this, one of the half-cream dried-milk preparations (see p. 298), to which is added half a drachm (2 gm.) of sugar for each 3 oz. (100 c.c.) of the feed, should be given at three-hourly intervals, one feed during the night being omitted. Certain anti-spasmodic drugs have been used with success. Eumydrin (atropine methyl nitrate) given in doses of 2·5 to 5 c.c. of a 1:10,000 solution half an hour before each feed is probably the best. It is more efficacious than atropine sulphate, is fifty times less poisonous and is now available in the form of lamellæ (pylostropin) which can be placed under the tongue. Over-dosage causes the skin to become dry and there may be some rise in temperature. If these symptoms become unduly pronounced, the drug should be omitted before one or two feeds or the dose reduced.

*Hypertrophic Pyloric Stenosis.*—Opinion is divided regarding the relative merits of surgical and medical treatment of this condition. In our opinion both forms of treatment have a place. If there are facilities for prolonged and rigid isolation and efficient nursing, medical treatment can be carried out with success, but failing this and especially if the services of an experienced surgeon are available, operative treatment is to be recommended. Although we are in favour of operative treatment in the majority of cases, there are circumstances in which medical treatment should be adopted. In the presence of respiratory or gastro-intestinal infections or of skin sepsis operation is contraindicated, and in the child who is brought for advice when eight or nine weeks old one is justified in endeavouring by non-operative measures to tide him over the comparatively short period of three or four weeks when spontaneous cure will occur, rather than subject him to the risks of operation.

The chief objection to medical treatment of the three or four-weeks-old infant is that it has to be continued for many weeks, during which time the enfeebled and emaciated patient may succumb to some intercurrent disease. This danger is specially to be feared in hospital practice where isolation cannot as a rule be carried out as efficiently as in the private home.

Where surgical treatment has been decided upon the best results are obtained when the physician is responsible for both the pre-operative and post-operative treatment. It is generally recognized that the greater the degree of emaciation and dehydration the less the chance of recovery. It is therefore of the utmost importance that the diagnosis should be made as soon as possible after the onset of symptoms and before emaciation has become severe.

Once the diagnosis has been made the operation should be performed without further delay, though when there is severe dehydration it may be deferred for forty-eight hours or longer. During this pre-operative period, treatment consists in measures aimed at restoring water and chloride to the infant's depleted tissues and in combating the alkalosis which is always present. In cases where dehydration is severe, plasma or a solution of 5 per cent. glucose in half-strength saline should be given by intravenous drip for a period of 12 to 24 hours. During this time 150 c.c. to 300 c.c. can safely be given. At the same time 60 c.c. of glucose saline may be given by the rectum at four-hourly intervals. If intravenous infusion is impracticable, normal saline solution may be given subcutaneously by the drip method. Any septic focus should be attended to, and special care should be taken to ensure that the umbilicus is soundly healed. Both before and after operation the child should be guarded in every possible way from respiratory infection. He should be isolated from other children, and no one with any respiratory infection such as coryza or pharyngitis should be permitted to come near him. The stomach should be washed out daily with normal saline solution. Lavage with sodium bicarbonate solution is contraindicated.

The Rammstedt operation is the operation of choice. Two hours after operation the child should be given saline solution or water by the mouth, followed two hours later by 4 drachms (15 c.c.) of one of the half-cream dried-milk preparations (see p. 298). During the next twelve hours water or saline alternating with the milk feeds in the above quantities should be given at two-hourly intervals. For the twelve hours thereafter double the quantity

of saline and milk should be given at the same intervals. Twenty-four hours after the operation the child should be given 2 oz. (60 c.c.) of the feed seven times a day at three-hourly intervals, missing one feed during the night. The quantity of the feeds should then be gradually increased, and about ten days after the operation their number should be reduced to five in the twenty-four hours. Sugar should be added with caution. For two or three days after operation, saline by the rectum at four-hourly intervals is extremely valuable but may not always be retained; if there are signs of dehydration, fluid should be given parenterally. In very feeble infants blood transfusion may be of benefit. The danger of wound infection is very great in these infants and this should be most carefully guarded against.

Medical treatment consists in the administration of a suitable diet (one of the half-cream dried-milk preparations with added sugar), gastric lavage once or twice daily with normal saline and the use of some anti-spasmodic drug. Eumydrin (atropine methyl nitrate) is probably the best of these and should be given in doses of 2.5 to 5 c.c. of a 1:10,000 solution half an hour before each feed. The correction of the dehydration and chloride loss is of primary importance. For the first two or three days half-strength saline should be given freely by the mouth and, if necessary, parenterally, but it must be remembered that oedema may appear before the chlorides in the urine return to normal.

**Vomiting in General Disease.**—In children, vomiting very commonly occurs in general disease in which the stomach is not primarily at fault; thus in pneumonia and pyogenic infection of the urinary tract it is often a prominent symptom. In these circumstances the treatment is that of the causative disease, but in infants care must be taken not to give too large feeds of milk, and it is usually wise to reduce its fat content by one of the recognized methods (see p. 298). Vomiting in conjunction with obstinate constipation should always raise the suspicion either of intestinal obstruction, *e.g.*, intussusception, or of increased intracranial pressure, *e.g.*, meningitis; here, also, the treatment is that of the primary cause. Conversely, cyclic vomiting (see p. 306) may also give rise to symptoms suggestive of acute abdominal or cerebral disease.

### CONSTIPATION

In infants and young children the most usual cause of constipation is insufficient food. The treatment consists in adjusting the diet. It is also commonly seen in cases of pyloric stenosis and meningitis in which the associated vomiting causes reduction in the amount of food entering the intestines. It rapidly passes off if the causative disease can be remedied. In this connection it should be mentioned that when there is great reduction in the amount of food entering the intestine, small, dark, rather loose slimy stools may be passed (starvation stools) and the mother may state that the child is suffering from diarrhoea. The stools consist largely of desquamated bowel epithelium, mucus, bile pigments and salts. Spasm of the anal sphincter, usually due to anal fissure, is sometimes a cause of constipation. The treatment consists in keeping the motions soft by suitable laxatives, *e.g.*, liquid paraffin emulsion and agar (B.P.C.), and, in the case of fissure, applying an ointment of ichthyol and tannic acid, in the proportion of 1 drachm (4 gm.) of each to 1 oz. (30 c.c.) of vaseline, to the part on a pledget

of cotton-wool inserted into the anus. In many cases of anal spasm relief may be obtained by stretching the sphincter.

### GASTRO-ENTERITIS

Though dietetic errors may be a predisposing cause, gastro-enteritis should be regarded as an infection. In its severe forms treatment must be prompt and energetic if life is to be saved. The main objects are to combat the toxæmia and to relieve dehydration and acidosis. Collapse may be severe, and in this case fluid must be given without delay either by the subcutaneous, intravenous or peritoneal routes. The child should be placed in a warmed cot, and if the temperature is subnormal heat should be applied by carefully guarded hot bottles or an electrically heated cage or blanket. As soon as the child's condition permits, the stomach should be washed out with a solution of bicarbonate of soda (1 teaspoonful to 1 pint) and the rectum with normal saline solution. Nothing but water should be given by the mouth for twelve to twenty-four hours and the child should be encouraged to drink as much as possible.

As regards the all-important question of diet a bewildering variety of milk mixtures and other foods has been advocated, such as protein milk, curd mixture, lactic acid milk, peptonized milk, glucose, albumin water, apple purée and sweetened tea. Description of the method of preparation of some of these is given on p. 299. After trying many of these preparations we have come to the conclusion that a diet of half-cream dried milk (No. 1 Ostermilk, half-cream Cow & Gate or half-cream National Dried Milk) is as effective as any of the more complicated formulæ and has the advantage of being simple to prepare. After the preliminary period of starvation small feeds of one of the half-cream preparations should be given at four-hourly intervals. Commencing with a feed of half an ounce the amount should be gradually increased until the child is receiving the quantity suitable for his age. In order to ensure that sufficient fluid is taken, water should be offered at frequent intervals. The fluid intake should amount to at least  $2\frac{1}{2}$  ounces per pound (150 c.c. per kg.) of body-weight in 24 hours. When there is serious loss of fluid from vomiting or diarrhoea or if the child refuses drinks, parenteral fluid must be given, preferably by the continuous-drip method. After the acute symptoms have passed off the greatest care with feeding must be observed, as relapse is very liable to occur if any liberties with the diet are taken.

Medicinal treatment is of little value, though sulphaguanidine seems to give satisfactory results in some cases, especially in those infected with dysentery organisms. Its use is still under trial. In children under one year 1 gm. per 5 lb. (0.5 gm. per kg.) of body-weight per day may be given in divided doses. If the child comes under observation soon after the commencement of the illness, 1 teaspoonful of castor oil may be given. In collapse, brandy is sometimes of benefit, while if there is great restlessness, or if convulsions occur, chloral hydrate in doses of 2 to 3 gr. (0.1 to 0.2 gm.) promotes sleep and depresses nervous irritability. Grey powder, the popular panacea for all infantile ailments, is of no value and is often harmful.

In the less acute forms where gastro-intestinal disturbance may have been present for some days or weeks it is not advisable to subject the child to too rigorous starvation, and after taking steps to replenish the depleted



tissues with fluid by one of the recognized methods, small feeds of diluted milk may be started immediately. In these subacute cases relapse is particularly likely to occur. The gastro-intestinal tract seems to be able to digest only very small amounts of the simplest food, and whenever the diet is raised in quantity to a level sufficient to allow of a gain in weight, diarrhoea and vomiting recur. It is in intractable cases of this sort that we see the typical picture of marasmus or atrophy. Here we have to guard against enteral infection by a most careful feeding regimen and against parenteral infection by scrupulous attention to nursing hygiene. When gastro-intestinal disturbance has been of long standing, iron-deficiency anæmia is almost inevitable. This should be treated by blood transfusion during the infection or with appropriate doses of iron and copper during convalescence.

### ACUTE ILEOCOLITIS (DYSENTERY)

Though dehydration is not as severe as in acute gastro-enteritis, toxæmia is as a rule very pronounced in ileocolitis and indeed the disease is occasionally fulminating in character. It may be necessary, however, to administer fluid by one of the recognized routes. As vomiting does not usually occur, gastric lavage is seldom necessary. With a view to freeing the large bowel of muco-pus, magnesium sulphate in repeated doses should be given by the mouth. In a child of six months 15 gr. (1 gm.) at hourly intervals for three or four consecutive hours will as a rule produce watery motions. This may be repeated daily for three or four days, by which time passage of blood, mucus and pus in the stools will probably have ceased. Tenesmus and colic are greatly relieved by this treatment. As the Flexner or Sonne organisms are commonly the causative agents, treatment with the appropriate serum has been advocated. The serum is injected intramuscularly in doses of 10 to 20 c.c. daily for several days. In our experience we have not found this form of treatment of any great value. Recently treatment with sulphaguanidine instead of magnesium sulphate has been found to give satisfactory results. The dosage for young children is the same as for gastro-enteritis (see p. 296). The diet should at first consist of half-cream dried milk. Commencing with 1 oz. (30 c.c.) at four-hourly intervals, the feeds may be gradually increased in quantity and strength as improvement in the condition of the stools occurs. As much water as the child will take should be given in the intervals between the feeds.

In the home, strict precautions should be taken to avoid infection of other members of the family, and in institutions such precautions are doubly important.

### CELIAC DISEASE

Of all the chronic diseases of childhood coeliac disease is probably the most difficult to treat successfully. Its essential chronicity, the tendency to relapse and the peevish and neurotic state of the patient impose an unenviable ordeal on the parents and medical attendant. As soon as the diagnosis is established, the nature of the disease should be explained to the parents, and it should be made clear to them that treatment will have to be continued for years before complete cure can be expected. The treatment is largely dietetic. As failure to absorb fat is the essential feature, and as the presence of this unabsorbed and decomposing fat in the bowel leads to general upset of the digestion, the first essential is to diminish the



fat content of the food to a minimum. In the early stages carbohydrate must also be reduced. Associated with the general intestinal upset there is defective absorption of important vitamins and minerals, and this feature of the disease must not be overlooked.

To commence with, the diet should be restricted to skimmed milk, especially if there is diarrhoea. As the stools improve, over-ripe mashed banana may be added to the diet, then calf's-foot jelly sweetened with saccharin. After a variable period of two to six months, sieved fat-free meat may be allowed, then dextrinized or malted foods, such as corn flakes, Horlick's, Mellin's Food, may be added gradually. Only when convalescence appears to be fairly well established should the fat be increased, and that with the greatest caution. Throughout the whole course of treatment a teaspoonful of orange juice should be given daily as well as some non-oily form of vitamin D, such as calciferol (B.P.) pellets in doses per day equivalent to 3 drachms (12 c.c.) of cod-liver oil (1,000 I.U. vitamin D) or, as a substitute, irradiation with ultra-violet light may be used to supply the necessary vitamin D. Anæmia is an almost constant finding, usually of the hypochromic variety; for this 1 to 3 gr. (0.06 to 0.2 gm.) of ferrous sulphate thrice daily should be given. In the event of the anæmia being hyperchromic, one of the liver extracts which can be given by injection should be used. Marmite, a teaspoonful twice a day, may also be of help. The child should be confined to bed in the early stages and in the relapses which so frequently occur, and the greatest care should be taken to guard him from intercurrent infection. In severe cases it may be necessary to give blood transfusions or saline and glucose by one of the recognized routes. If tetany should develop, 5 c.c. of calcium gluconate should be injected intramuscularly or into a vein and vitamin D pushed. Crude liver extract and vitamin B complex given on alternate days have been recommended, but the results are not very encouraging. Folic acid can only be regarded as helpful in the treatment of coeliac disease when there is macrocytic anæmia associated with a megaloblastic bone marrow. In these circumstances the anæmia may be corrected by giving 10 mg. of the drug by the mouth daily.

Should relapse occur a return must be made to the original diet and the whole process of gradually building it up must be gone through once more. The success of the treatment depends largely on the intelligent co-operation of the parents.

### MILK MODIFICATIONS

**Dried Milks.**—Dried milks are now widely used in infant feeding, and have certain advantages over liquid milk. They are free from pathogenic organisms, are constant in composition and can be kept for long periods. Though some are expensive there are suitable brands, such as the National Dried Milk supplied by the Ministry of Food, which can be purchased at a moderate cost. Usually two preparations, half-cream and full-cream, are marketed. In certain proprietary preparations iron or vitamin D have been added. As a rule one "measure" (a rounded teaspoonful) of the powder is the amount required to make one ounce (30 c.c.) of reconstituted milk. Sugar can be added in the same way as to liquid milk.

**Milk Containing a Low Percentage of Fat.**—Milk separated by centrifugalization contains about 0.5 per cent. fat. The percentage of fat may be increased by adding a proportion of the separated cream.

Reduction of the fat may also be obtained by allowing a pint (600 c.c.) of milk to stand for four hours and skimming off the "top milk." If the top 12 oz. (350 c.c.) are removed the residue contains about 1 per cent. fat; if the top 8 oz. (230 c.c.) are removed it contains about 2 per cent. fat. Dried-milk preparations containing a low percentage of fat can be purchased.

**Peptonized Milk.**—Dissolve one peptonizing powder (Fairchild) in 5 oz. (150 c.c.) of water. Add this to 1 pint (600 c.c.) of milk, warm gently to body temperature and allow to digest for twenty minutes; then bring to the boil and allow to cool rapidly.

**Lactic Acid Milk.**—Stir into 1 pint (600 c.c.) of milk 45 minims (3 c.c.) of lactic acid (B.P.). The acid should be added drop by drop whilst the milk is being vigorously stirred. An egg whisk is useful for this purpose.

## DISEASES OF THE RESPIRATORY SYSTEM

### INFECTIONS

Disease of the respiratory system is caused mainly by "droplet" infection and is one of the major causes of death in young children, especially in early infancy. Too much stress, therefore, cannot be laid on the prevention of infections of this nature. For example, any person with a head cold should, whenever possible, refrain from looking after an infant; this may, of course, not be practicable in the case of a nursing mother, but she should be instructed to wear a mask of gauze or preferably a mask with one layer of cellophane or blotting paper between layers of gauze when nursing or caring for her infant.

**"Colds."**—The commonest respiratory infection is a "cold," and this may manifest itself in various ways: a nasal discharge, redness of the pharynx, tonsillitis, otitis media or cough. In all young infants, and especially during the neo-natal period, upper respiratory infections should not be treated lightly. The patient should be confined to his cot in a cool room at a temperature between 60° and 65° F. and abundant fluid supplied. If fever be present the diet should be fluid, and in infants it is best to dilute the milk as their tolerance to food is usually diminished. If diarrhoea and vomiting are prominent features, treatment as for gastro-enteritis may be adopted, though the diet need not be so drastically restricted as in true gastro-enteritis. Local treatment for the throat is probably not advisable; if the nasal passages are obstructed a few drops of liquid paraffin containing 2 gr. (0.12 gm.) each of menthol and camphor to the ounce (30 c.c.) may be instilled into each nostril ten minutes before feeding time. The head should be held slightly back to allow the liquid paraffin to run into the nasopharynx. This clears the nasal passages, thus enabling the infant to breathe through the nose whilst sucking. If the cervical glands become involved it is advisable to protect them with a collar of gamgee.

**Otitis Media.**—The danger of spread of the throat infection to the middle ear must always be borne in mind. It is possible that this danger may in some degree be lessened if care is taken to have the infant nursed in the semi-erect position. This is particularly necessary whilst he is taking his feeds, for during the act of swallowing the pharyngeal orifice of the Eustachian tube gapes and may permit the entrance of infected material. In the event of infection occurring, a few drops of glycerin of carbolic (half

strength of the B.P. formula) should be instilled into the auditory canal. This is useful in relieving pain. The efficacy of sulphonamides in otitis is still debatable. It is claimed by some authorities that if pus has formed in the middle ear, treatment with sulphonamides relieves the immediate symptoms but gives a false sense of security as the infection may be silently spreading into the mastoid antrum. In our experience, however, we have not observed an increase in the incidence of mastoiditis since we commenced to use these drugs in the treatment of acute upper respiratory infections. The tympanic membrane should be examined frequently and, if found to be bulging, incised. The introduction of the electric auriscope has greatly simplified this procedure.

**Bronchitis and Pneumonia.**—Upper respiratory infection may also spread to the lower respiratory passages, giving rise to bronchitis and broncho-pneumonia and adding to the gravity of the situation. It is often difficult to differentiate severe bronchitis from broncho-pneumonia, and in any case the treatment of both conditions is on similar lines.

**Nursing.**—Skilled nursing is the first requisite. The child should be nursed in a well-ventilated room kept at a temperature of about 60° F. Nursing out of doors on a balcony or with the cot placed beside a wide-open window regardless of climatic conditions has yielded good results. The clothing must be loose, especially round the neck. Tepid sponging, when the skin temperature exceeds 102·5° F., tends to the general comfort of the child and promotes sleep. Drinks of water or diluted fruit juice should be offered frequently in addition to the regular feeds. The child should be allowed to lie in the position in which he seems most comfortable, but it must be remembered that young children should not be permitted to remain in one position for too long a time. The diet should consist of diluted milk sweetened with sugar, which should be given at three-hourly intervals. In the presence of gastro-intestinal disturbance the amount of sugar in the feeds should be restricted.

**Cough.**—Cough can be a troublesome symptom and in very young infants it is probably unwise as well as useless to prescribe expectorant mixtures. A sedative, however, is often advisable. Fifteen to thirty minims (1·0 to 2·0 c.c.) of syrup of codeine to an infant of six months, and repeated if necessary, or chloral hydrate gr. 3 (0·2 gm.) will often produce a cessation of a troublesome cough and induce sleep. When secretion is abundant and the finer bronchi and bronchioles become obstructed, atropine in doses of  $\frac{1}{160}$  to  $\frac{1}{200}$  gr. (0·4 to 0·3 mg.) should be given hypodermically at four-hourly intervals, or tincture of belladonna by the mouth in doses of 2 to 5 minims (0·12 to 0·3 c.c.). Stimulants may be required; brandy four-hourly is valuable, and camphor in oil in doses of 10 to 15 minims (0·6 to 1 c.c.) has been recommended, though in our experience it has not proved of much avail. Elixir of ephedrine in doses of  $\frac{1}{2}$  drachm (2·0 c.c.) at four-hourly intervals helps to dilate the finer bronchi and acts as a vasomotor stimulant. Strychnine and digitalis are better avoided.

Steam as an inhalant is sometimes of use when there is respiratory distress with a dry cough, severe stridor and difficulty in getting rid of bronchial secretion. In some cases its effect is dramatic in alleviating cough and inducing rest, in others it has the opposite effect, and in these circumstances should not be continued. A satisfactory tent can be devised by placing a screen round the head of the cot and covering this with a sheet,

leaving the side facing the foot of the cot open. Steam generated in a special kettle fitted with a funnel measuring  $2\frac{1}{2}$  ft. in length is allowed to flow gently into the tent. It may be medicated by adding 1 or 2 teaspoonfuls of tincture of benzoin co. to the water in the kettle. The funnel should be adjusted so that there is no possibility of the steam impinging directly on the patient. The greatest precautions against fire must be taken. The funnel must be long enough to permit the kettle with its spirit lamp to be placed well away from the cot. Steam should not be used continuously, but only for a half or one hour every two hours. Occasionally it excites the patient or he fails to get any relief, and in such circumstances it should be discontinued. Some authorities regard its value as doubtful; it is the antithesis of fresh-air treatment, and its use carries a risk of fire or burning which would not otherwise exist.

If there is reason to suspect pain on coughing, a poultice may be applied over the affected part of the lung. It is always well to warn the mother against the danger of burning the skin. If mustard is used, a concentration of 1 to 6 parts of linseed meal for infants and 1 to 4 for older children is suitable. After anointing the skin with olive oil, the poultice may be allowed to remain on the chest for twenty minutes to half an hour with safety.

**Cyanosis.**—If cyanosis is present, oxygen is indicated; nowadays this can be given readily by means of a small oxygen tent. Several types are available. One we have found to be satisfactory is manufactured by the Condensed Gas Company, Manchester. Oxygen should be run in at the rate of 8 litres per minute. Failing a tent, oxygen may be given through a small rubber catheter inserted to a distance of 1 to 2 in. into the nostril. The rate of flow should be 3 to 4 litres per minute. (For details of oxygen therapy see p. 954.)

**Specific Treatment.**—As there is great variation in the type of pneumococcus responsible for pneumonia in young children, serum treatment is not to be recommended. In older children, many of whom are infected with Types I or II, the disease is so benign that serum therapy is as a rule not called for. In any case there is every reason to believe that suitable sulphonamide preparations are equally efficacious and should be used in all serious cases. Even young infants tolerate the drug well. The only difficulty encountered with any frequency is vomiting; when this is serious and the grave state of the patient demands heroic treatment, the soluble preparation, sodium sulphathiazole, may be given in glucose saline intravenously. If administration of a sulphonamide by intramuscular injection is desired, a neutral preparation such as soluthiazole (M. and B.) will be found satisfactory. Pneumonia due to staphylococcal infection is of fairly frequent occurrence in infants under three months of age. In these cases penicillin should be used. As the disease in these young children runs a very rapid course and is very fatal, treatment should be instituted promptly and without waiting till bacteriological evidence of the causative organism is obtained. In infants under three months of age, penicillin by mouth in doses of 5,000 to 10,000 units three or four-hourly will provide adequate blood-levels. Over this age it is best given by intramuscular injection.

**Empyema.**—In the event of empyema developing, it is best in the first instance to persist with paracentesis combined with the local use of penicillin (see p. 92). Paracentesis should be carried out at intervals as indicated by the

physical signs and the temperature. Empyema is never a surgical emergency requiring immediate radical treatment. In infants under one year, conservative treatment by aspiration is likely to yield much better results than the more drastic procedures. In older children, however, when aspiration of the pus proves ineffective, the condition should be dealt with surgically. It is important to pay attention to the general health of small infants with empyema. Many of them develop severe anæmia and, as iron in the presence of such an infection is ineffective, blood transfusion may be required.

**Pulmonary Fibrosis and Bronchiectasis.**—Most frequently this is the sequel to a pneumonia which has failed to resolve or to pulmonary collapse. Much can be done for such patients but improvement is slow, and in well-marked examples of the disease it must be recognized that cure in the sense of the lung returning to normal is impossible.

General hygienic measures are important, and the greatest care should be taken to prevent respiratory infections. Abundant fresh air and a country life are of advantage, especially prolonged residence in a dry climate. In the event of a flare-up of the lung condition, treatment with sulphathiazole is useful in allaying the acute symptoms. Foci of sepsis in the sinuses or the tonsils should be dealt with. The antra are particularly liable to be affected and special attention should be paid to the examination of this part of the respiratory tract.

Two valuable methods of treatment are postural drainage and deep-breathing exercises. Every morning on rising, the patient should be placed over the side of a bed or a chair with the head hanging down and be made to cough up as much sputum as possible. If much is obtained, this procedure should be carried out twice or even three times daily. Alternatively the child may be placed face downwards on a double inclined plane (Nelson bed) and kept in this position for an hour two or three times a day. In any case, it is important that the bronchi should be emptied as thoroughly as possible. Following this, the patient should be instructed to breathe slowly and as deeply as he is able for a period of five minutes. If it can be arranged, it is best to have an adult do this exercise with the child. With patience even very young children can be taught these exercises satisfactorily.

Creosote, given by the mouth, inhalation of this or of iodoform and eucalyptus from a mask or of penicillin from an atomizer and autogenous vaccines have been advocated, but their benefit is doubtful.

In certain cases in which less drastic measures have failed to bring about amelioration, resort should be had to surgery. Recent advances in the technique of thoracic surgery have made it possible to remove a part or the whole of a lung with good prospect of success. The extent of the disease must first be clearly defined by means of X-ray examination following lipiodol injection to outline the bronchial tree. After a period of medical treatment, and when the general condition of the patient warrants it, the affected lung or part of lung is removed. The operative risk has diminished considerably in recent years, and it is now recognized that young children are even better subjects than adults; nevertheless the cases should be carefully chosen. Phrenic evulsion in certain cases in which lobectomy is impracticable may be considered. Artificial pneumothorax has been advocated, but in many instances, owing to pleural adhesions or because of the firm fibrotic nature of the lesion, it is not attended by any great degree of success.

### ATELECTASIS

Failure of the lung to expand (atelectasis) is seen in very young children. Inhalations of oxygen with 10 per cent. carbon dioxide by means of a nasal catheter or a small tent are of great value. Quietness, rest and, if necessary, stimulants such as brandy or lobelin, in doses of  $\frac{1}{8}$  gr. (0.01 gm.), are indicated. In many instances the atelectatic lung becomes infected, and as far as treatment is concerned the lesion becomes virtually broncho-pneumonia.

### THYMIC ENLARGEMENT

The subject of thymic enlargement and status thymicolymphaticus is a most debatable one. Stridor, syncope and dyspnoea, cyanotic attacks or fits may be manifestations of the condition, and direct evidence of thymic enlargement may be obtained by the detection of dullness at the upper end of the sternum or by X-ray examination. If the existence of an enlarged thymus is established and it is giving rise to symptoms, radiotherapy in the hands of an expert should be employed.

## DISEASES OF THE NERVOUS SYSTEM

### CONVULSIONS

A convulsion is probably the commonest medical emergency in childhood. In the first instance efforts should be directed towards controlling the attack. There is general agreement that the hot bath or mustard bath (temperature 105° F.) is worth while if only to keep the mother or nursemaid occupied. If an anæsthetic such as chloroform or ether is available, its administration is the surest way of controlling the spasm. Chloral hydrate is satisfactory, although it takes some time to produce its effect. If the child can swallow, a dose of 3 to 5 gr. (0.2 to 0.3 gm.) to a child of one to two years should suffice; subsequently smaller doses may be repeated four-hourly. If he cannot swallow, double the above dose may be given by the rectum. Some prefer to combine this with bromide, but there does not appear to be any particular advantage in doing so. If the fit has continued for some time and a condition such as status epilepticus is threatened, morphine  $\frac{1}{4}$  gr. (2.5 mg., for a child of two years) given by hypodermic injection, or paraldehyde in doses of 1 drachm (4 c.c.) of paraldehyde in olive oil per stone of body-weight by the rectum, is effective. It is frequently wise to perform a lumbar puncture for, if there are signs of meningitis, it is essential for diagnosis and subsequent treatment, although its value in controlling the convulsions may not always be apparent.

It is important to remember that having controlled the convulsions in the first instance it is necessary to guard against their recurrence during the next few days. For this chloral hydrate is the most useful drug, as it is rapidly eliminated and non-cumulative in its action. The dose and frequency should gradually be diminished during the succeeding three or four days.

To treat any case of convulsions intelligently one must ascertain the cause. The idea that sources of peripheral irritation such as teething, worms, constipation (or diarrhoea), adherent foreskin, enlarged tonsils and so forth are commonly the cause of fits is untenable. Such a suggestion may be comforting both to the physician and the parent in so far that one need

never be at a loss to discover some source of peripheral irritation, but actual proof of their association as cause and effect is lacking. Actually convulsions in children may be classified under three main headings: those due to hypocalcæmia, those due to intracranial injury or disease, and a group of unknown ætiology (idiopathic convulsions). Of these the convulsions due to hypocalcæmia are undoubtedly the most common. Other clinical signs of hypocalcæmia, such as tetany, may or may not be present, but not infrequently the only manifestation will be the convulsion. This is the case in many instances where the convulsion ushers in an acute infection, and more likely is this to be so in the late winter and spring months when the incidence of tetany is at its maximum. Hypocalcæmic fits are readily controlled by chloral hydrate. For a child of one year an initial dose of 4 gr. (0.25 gm.) should be given, followed by 1 gr. (0.06 gm.) every two hours until he is thoroughly under the influence of the drug. Five cubic centimetres of 10 per cent. calcium gluconate solution (Sandoz) given intravenously or intramuscularly, by raising the blood calcium rapidly, will accomplish the same object; thereafter by the administration of a suitable vitamin D preparation (approximately 1,000 units daily), the retention of calcium can be restored to normal and maintained at this level. The sedative or the calcium gluconate should be continued for three days, by which time retention of calcium will be adequate. The antirachitic treatment must be continued for several months to prevent relapse. The blood calcium can also be quickly restored to normal and so prevent the possible recurrence of the fits by the administration of an acid-producing salt such as calcium chloride or ammonium chloride. These salts may be given to infants in doses of 15 to 30 gr. (1 to 2 gm.) four-hourly, and by producing a compensated acidosis cause an increased amount of calcium to remain in solution in the blood stream. Here, too, acid treatment is only required for three to four days, but the antirachitic therapy which should be given along with it must be continued, as previously mentioned.

The group of convulsions frequently referred to as idiopathic, occurring later than the age of the cerebral birth trauma and earlier than that of frank tetany—i.e., from second to fourth month—are also mainly hypocalcæmic in origin and may be treated successfully with chloral hydrate and vitamin D, as described above. One would emphasize the importance of diminishing the dose of chloral slowly once the condition has been brought under control.

Convulsions in the newborn, whether the result of cerebral birth trauma or not, should be treated with chloral hydrate four-hourly in doses sufficient to control them. A bulging anterior fontanelle points to the necessity of relieving the intracranial pressure by lumbar or ventricular puncture, procedures which may have to be repeated.

Convulsions which have been recurring over a period of weeks or months, such as those seen in mentally defective children and potential epileptics, are best treated with some sedative which can be continued over a long period. For this phenobarbitone or phemitone will be found suitable. A child of two or three years can safely be given  $\frac{1}{2}$  gr. (0.03 gm.) of phenobarbitone twice daily or double this amount of phemitone.

Finally, in all cases attention must be paid to the presence of other disease. Constipation should be treated, for while it may not be an ætiological factor, it tends to aggravate the condition.



Breath-holding attacks should never be treated lightly, as seizures of this nature may end in true convulsions associated with loss of consciousness. The condition is said most commonly to be seen in spoilt only children; this may be so, but it does not minimize the seriousness of the attack. With firm treatment, avoidance of "scenes" and the judicious use of a sedative, such as phenobarbitone, a satisfactory outcome can be expected.

### MENTAL DEFICIENCY

In the treatment of mental deficiency a proper understanding of the ætiology is important. Approximately half the cases may be included under the heading simple amentia, one-quarter are Mongolian imbeciles, and of the remainder such conditions as cretinism, amaurotic family idiocy, birth trauma, meningitis, encephalitis, etc., are responsible for the defect. The treatment of all save the cretins can only be palliative. As a general rule it is not advisable bluntly to tell the mother that her child is mentally defective. The phrase should be avoided in discussing the problem with her. It must be explained that the child is backward and will be difficult to bring up, but that the progress depends to a great extent on her efforts to educate him. With patience and unflinching care on the part of the mother many of the less afflicted children may be taught to feed and clothe themselves, to be cleanly in their habits and probably to perform simple household duties. As the child grows older it may be possible to send him to a special school where association with other children helps to stimulate his mental faculties. He should not be sent to school with normal children, for he is apt to be bullied and his sense of inferiority is increased. The child must be guarded from injury, convulsions may be controlled by sedatives, and where home conditions do not permit of proper care, institutional treatment is advisable. In certain cases of cerebral diplegia, orthopædic measures which succeed in enabling the child to walk may lead to improvement in the mental condition.

**Cretinism** is the only form of mental deficiency where treatment holds out the hope of definite cure. Cretinism and Mongolian idiocy must be clearly differentiated. Thyroid has been recommended for the latter, but in our experience it is valueless. For the treatment of cretinism see p. 420.

### ENURESIS

Before commencing the treatment of this troublesome complaint it is essential that the presence of organic disease be excluded. The urine should be carefully examined for albumen, pus and sugar. Renal dwarfs, for example, often come under observation because of nocturnal incontinence, and if there is any dwarfing or sign suggestive of impaired renal function, the blood urea should be estimated. In other cases the condition is simply due to faulty education on the part of the parents. Cases of this nature are chiefly met with among the lowest classes. Here treatment consists in educating the child in ordinary habits of cleanliness. True enuresis is essentially a functional disease.

Many forms of treatment have been recommended, and it may be said at once that no one method is likely to succeed in more than a small percentage of cases. The principle of obtaining "dry nights" over a prolonged period of time by the simple expedient of getting the patient up to pass



urine as frequently as is necessary is often effective. The child should be made to empty his bladder just before going to bed, an hour or two later and once between then and waking in the morning. After a month or two of "dry nights," the wakening in the early hours of the morning should be omitted. Relapses may occur and accidents will happen from time to time which may lead to abandonment of the treatment, but the parents should be encouraged to persevere, as their wholehearted co-operation is an important part of the treatment. Apart from the inconvenience entailed, which is not often an objection, the greatest drawback is the sleep lost by the child. It is as well to instruct the parents that they should never discuss his shortcoming in his presence nor show any undue concern. Scolding and punishment are to be deprecated. Too often his anxiety not to wet the bed is his undoing, and constant reminders in the form of encouragement or the reverse from the parents or nurse only serve to keep his affliction in the forefront of his thoughts. Such children are often unduly sensitive and punishment may be a prominent factor in keeping up the condition.

Whatever other treatment is adopted it is important that no fluid nor food should be given within two hours of bedtime. The general health must be seen to. Enlarged tonsils and adenoids may require removal. Rest must be adequate and, if possible, a rest in the middle of the day obtained. All undue fatigue and emotional disturbance are best avoided. The bedclothes should not be too heavy, and it may be of value to provide some device, such as a towel tied around the waist with the knot in the back, to prevent the child from lying on his back. Drug therapy is not of much value. Small doses of thyroid extract have been used by some. Others claim success with eserine. Belladonna, however, has the widest reputation, and its use with other methods can be recommended. Commencing with 5 to 10 minims (0.3 to 0.6 c.c.) of the tincture thrice daily, the dose should be increased until moderate dilatation of the pupils and dryness of the mouth indicate that the child is fully under the influence of the drug.

In intractable cases, and in mentally deficient children in whom it is impossible to obtain co-operation, the use of sphagnum moss is of value in making the nursing and care of these children less arduous. It can be placed under the child and between the thighs against the genitals at night. The urine is absorbed by the moss and the sheets are kept dry. The urinous odour which is so objectionable is also to a great extent dispelled.

### CYCLICAL VOMITING

The ætiology of this condition is somewhat obscure and its diagnosis often open to criticism. There are varying shades of opinion as to what constitutes the clinical picture. Infection, often trivial, and emotional upset are regarded as the two most common predisposing causes. The outstanding clinical feature is the occurrence of more or less periodic attacks of intractable vomiting during which there is a marked ketosis and in most instances an acidosis. The age incidence is roughly from the second to the seventh year. The subjects of the disorder are often highly strung children. There may be a history of infantile eczema and later, asthmatic attacks or migraine are not uncommon.

\* The attack begins fairly abruptly after a few hours of lassitude. Dark rings appear under the eyes and vomiting sets in, even water being returned.

The administration of water or saline with glucose and alkali are indicated. This can be accomplished readily by giving glucose in water or saline flavoured with orange or lemon juice by mouth. Big drinks are likely to be returned, and only sips from a spoon at frequent intervals should be given. It may be necessary to detail some person to be constantly in attendance for this purpose. Although much of the fluid may appear to be vomited, if the method is persisted with, a considerable amount will remain in the stomach and eventually be absorbed. The water and salt combat the dehydration and the glucose helps to control the production of ketone bodies. The best alkali to give is sodium bicarbonate. It should be dissolved in water and given separately in sips at the rate of 15 to 30 gr. (1 to 2 gm.) four-hourly. It aids in the excretion of ketone bodies, provides alkali and acts as a stimulant to the secretion of gastric juices.

In all but the most severe cases administration of fluid by mouth will suffice. But when the vomiting is intractable and the dehydration and ketosis persist, 10 per cent. glucose in saline given by rectum is of the greatest benefit. The bowel should first be washed out and then 2 to 4 oz. (60 to 120 c.c.) of the glucose and saline solution run in four-hourly. If the patient is markedly dehydrated and presents alarming signs of acidosis such as air-hunger and a low  $\text{CO}_2$ -combining power of the blood, it is advisable to give the 5 per cent. glucose in saline intravenously by the continuous-drip method.

During the period of active vomiting all food save glucose should be withheld. Four to six hours after the vomiting has ceased diluted milk or weak sweetened tea or oat-flour porridge may be given. Recovery as a rule is rapid and the diet can be quickly increased.

Between attacks, a high carbohydrate intake is recommended, and the amount of fat in the diet should be reduced. Rich foods such as pastry and suet puddings should be avoided. All fruit and vegetables, because of their alkaline ash, are permitted. Sugar, as cane-sugar, barley-sugar or "boiled sweets," can be allowed. It is well to point out to the mother that chocolate and toffee contain a good deal of fat. Glucose or glucose D, a tablespoonful after each meal, has been recommended. It is doubtful if it is wise to use it thus as a medicine. The children often object to it and it is a constant reminder of their affliction. Cream, cod-liver oil tonics and fried foods are often given in large quantities to such children in an attempt to fatten them. This is a mistake. Such substances are better avoided. Butter should be allowed in reasonable amounts and milk in the usual quantities.

In addition to this dietary régime, a small  $\frac{1}{2}$  teaspoonful of baking-soda (sodium bicarbonate) in water each morning before breakfast should be given as a stimulant to the digestive juices.

### PINK DISEASE

#### *(Erythrædema Polyneuritis)*

As the ætiology of pink disease is unknown the treatment is necessarily symptomatic. The first essential is to guard the child as far as possible from intercurrent infection. He should, whenever possible, live in good surroundings in the country. Institutional treatment is definitely contra-indicated. Relief from many of the distressing symptoms of the disease can to some extent be obtained by careful nursing. Thus the intensely

irritating sudaminous rash may be alleviated or prevented by ensuring that no flannel or woollen garments are placed next to the skin. The skin should be most carefully dried and powdered after bathing, and in some cases a soothing lotion such as

R7	Calamin.	.	.	.	.	.	dr. ii (8 gm.)
	Zinc. Oxid.	.	.	.	.	.	dr. ii (8 gm.)
	Phenol.	.	.	.	.	.	gr. x (0.6 gm.)
	Glycer.	.	.	.	.	.	fl. dr. ii (8 c.c.)
	Liq. Calc. Hydrox.	.	.	.	.	ad	fl. oz. iv (120 c.c.)

is useful in relieving irritation. The arms may have to be splinted to prevent scratching. When there is great irritation of the hands and feet, relief may sometimes be obtained by allowing the child from time to time to hold them in cold water. When photophobia is a prominent symptom it may be necessary to nurse the child in a darkened room or to provide an eye-shade. For sleeplessness sedatives such as chloral hydrate are necessary. The diet should be light and nourishing, and as anorexia is so commonly present the child must be coaxed to take his food and in some cases it may be necessary to feed by gavage. The child should be kept in bed at first, but as improvement takes place he may be taken out-of-doors in a perambulator. On the supposition that the disease is due to vitamin deficiency it may be advisable to give cod-liver oil or one of its substitutes, also orange juice and marmite or bemax. Though there is no proof that these accessory food factors have any direct effect on the course of the disease, they may be of help in improving the general condition of the child. The parents should be warned that the disease usually runs a course of three to six months and that during this time incessant care and vigilance will have to be exercised. Complications such as otitis media, pyuria, respiratory and intestinal infections must be watched for and treated as they arise.

G. B. FLEMING.

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## THE CARE OF OLD PEOPLE

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**INTRODUCTION.**—The dry statistics of old age in England and Wales show that in        under 10 per cent. of the population were people of pensionable age, that is, men of 65 and over or women of 60 and over; in        12.6 per cent. were of pensionable age; in        if present trends continue, the figure will have risen to 14.1 per cent., and in        to 15.8 per cent. In Scotland the proportions are similar.

For the general practitioner that means that a rapidly increasing number of his patients will be "old people." The opportunity presented to him, in the medical care of these people, deserves some study. It is twofold. First, he is obviously concerned to treat them when they are ill, and must therefore be familiar with the natural history of disease in the aged, for the incidence of various disorders and the manifestations of the same disorder differ widely in different age-periods. Secondly, and more importantly, the doctor is concerned with the maintenance of health in the old, a matter of great consequence to the individual and to the community.

**Structural and Functional Changes in Old Age.**—If we turn to anatomy and physiology for guiding principles in these tasks we get much information but little help. It seems to lie in the nature of things that a multicellular organism has a life-span during which it passes, by gradations so smooth as to form a curve, from youth to maturity and from maturity to old age and death. The physical continuity of the race is preserved only through the strong but tenuous link of the germ plasm. The outward anatomical changes of old age are familiar: grey and falling hair,<sup>1</sup> loosening teeth, dry and wrinkled skin, loss of subcutaneous fat, bowed back and shortened stature. Their common feature is a slow atrophy of tissues, with a decrease in their water content whereby they become harder and less resilient. Similar changes proceed in the internal organs: the pathologist finds senile atrophy of the viscera and the brain; stiffening of the lens causes presbyopia and atrophy of the eighth nerve endings in the cochlea restricts the audibility of high tones. The accompanying physiological changes are less evident in the functions of the body at rest than in its responses to stimuli. Changes in temperature, pulse and respiration rate, and in concentrations of blood constituents, at rest, are slight or absent. Mouth temperatures, indeed, are apt to lie below 98° F. and axillary temperatures below 97° F. in men over seventy. The basal metabolic rate has fallen to -10 per cent. at about sixty, and may fall further, even to -25 per cent., in extreme old age. But the conspicuous changes are in the reactions to stimuli: movements become slower; the capacity for physical exertion, both of the muscles and of the heart and lungs, diminishes; the maximum concentrating power of the kidneys is lessened; the body is less able to maintain its constant temperature in hot or cold environments. In short, the range of response of every organ and every physiological function is narrowed. The reproductive

<sup>1</sup> These may also have causes other than age.

function ceases in women at the menopause and in men dwindles at a later age.

The mechanism by which these anatomical and physiological changes of age are brought about is obscure. It is therefore impossible to explain why they proceed faster in some individuals than in others, and faster in some organs or functions than in others. No simple hormone defect underlies them, and no known hormone treatment counteracts them. Interwoven with them is the development of arteriosclerosis and atheroma, which slowly throttles the blood supply to organs and tissues, marring their structure and restricting their function. The cause of the vascular degenerations is unknown, but they are held to be pathological and not an intrinsic part of the process of ageing. Continued hypertension aggravates them, and they increase with time; otherwise their progress and their distribution seem to vary capriciously.

It has been observed by Oliver Wendell Holmes and many others that longevity in man is a family characteristic; in strains of mice it appears that the rate at which individual organs age is a strain characteristic. Clearly a hereditary factor is concerned in determining how fast men grow old; it may be the most important factor. But to say, as some have done, that every individual begins life with a certain stock of vital energy, the size of which, other things being equal, determines his life-span, is no more than to repeat that conclusion in other and vaguer words. Next to heredity we should expect environmental conditions to influence the rate of growing old—climate, shelter, food, physical exertion, past infections and the like; but proof of the influence of any one of these is difficult to come by, because it cannot be separated from the others.

The interdependence of the anatomical and the physiological changes of age is not clearly understood. No doubt the anatomical changes are in large measure primary; in the case of presbyopia and presbycusis they must be so. But how far may the stiffening of the legs and the weakening of the muscles be accelerated either by their over-use (as in the miner), or by their under-use (as in the sedentary individual)? In youth it is clear that within limits the exercise of a function brings about improvement in its performance and anatomical development of the organs concerned. If the same principle applies in old age, superimposed now on a fundamental trend that is decrescent instead of crescent, it is likely that there is an optimum use of functions—neither too much nor too little—that will prevent their failing too rapidly and keep the rate of anatomical change slow. Function depends on structure, but function also reacts on structure. Common observation suggests that this is so, though again proof is hard to obtain. To point to octogenarians who have remarkably exercised and preserved their faculties does not help, for the hereditary factor cannot easily be assessed. We assume the truth of the principle, and seek the optimum in the exercise of functions.

This anatomical and physiological discussion almost inevitably leads to academic speculation as to how life may be prolonged. Though it has hitherto yielded little increase of knowledge, the speculation has always fascinated writers on old age; one of them recently held the chief task of Medicine during the coming generation to be the extension of the human life-span. For the general practitioner, at least, this is a mistaken aim. His desire should be to see his fellows live fully rather than merely for a

long time. His effort should be to persuade old people into as much and as varied activity, mental and physical, as their powers allow. It must be such activity as brings them satisfaction; its limits will normally be set by natural fatigue. If the doctor can help the old to achieve this, he is maintaining their health. Not unlikely he is also and incidentally prolonging their days, but his emphasis should remain on the immediate aim of encouraging full and satisfying activity.

**Mental Changes.**—The curve of the development and decline of mental powers does not parallel that of physical powers. Its peak comes later. Footballers and fighter-pilots are past their prime at thirty; most kinds of mental activity show unabated vigour throughout middle life. The first sign of limitation is a narrowing of interest and a lessened receptivity for new ideas; thought and judgment, in familiar fields, are unimpaired, in strange ones a little hampered. Imagination plays a dwindling rôle. The outlook and way of thinking that were predominant in middle life become more fixed and rigid and exclusive. Then memory begins to weaken, at first capriciously and in trifling ways, later more obviously. Attention and concentration grow less intense. All the mental processes become gradually slower. Emotion seems to be less keenly felt and emotional "drive" diminishes.

These changes, in the sixties and seventies, are normal enough; if they do not occur, it is a matter for remark. In some old people, on the other hand, they lead on, by a sad acceleration, across the undefined boundary between normal and abnormal, into senile mental degeneration. The narrowing interest becomes an obstinate adherence to routine. Traits become so fixed and exaggerated that the patient's personality grows to be a caricature of his former self. Less and less enters his mind. Failure of memory for recent events sends his thoughts back into the past; it also confuses him in his attempts to deal with the present, and his inadequacy, dimly appreciated and struggled against, leads him into confabulation, or breeds suspicion and ideas of persecution in his mind. Irritability, restlessness (with wandering), or outbursts of anger and violence can result. Hallucinations may be added to delusions. Emotional depression and attempts at suicide are not uncommon. Or, when the regression follows a gentler course, an old person may spend long hours sitting in apathetic remoteness from what goes on around him, waking up for short surprising lucid intervals to take some notice and some part in conversation; mostly he will be biddable and easy to manage. At first he will show some distress at his physical clumsiness, his increasing forgetfulness and his difficulties with long sentences; later he will appear indifferent. Over years, sometimes interrupted by remarkable remissions, the slow deterioration progresses to the final dementia.

The physical basis of these changes is no doubt atrophy of the cerebrum. In some cases, but not in others, sclerosis and atheroma of cerebral vessels contribute through ischæmia to this atrophy. Clinically there is little to distinguish the mental deterioration of cerebral arteriosclerosis from that of "simple senile degeneration" except that the former is accompanied by thrombotic episodes or the physical signs of upper motor neurone damage. In the earliest stages, however, it is possible that the rate at which mental faculties decline is not solely dependent on the underlying physical changes, but can be influenced by the degree to which the mental faculties are used, and therefore by the extent to which the subject's psychological environment

stimulates his active response. It has been suggested that the conservatism of the old, their passionate clinging to familiar possessions and established routines, may depend not only on their realization that their powers are waning, but also on their realization that society has lost interest in them. When the paid worker retires, he gives up both his wage and his position of responsibility in the community; the sense of belonging and being expected to contribute to the community's life suddenly disappears. The whole cycle of stimulus, effort and reward ceases. The same thing happens to the married woman when she is widowed, especially if she has to live alone. Of both, in their retirement, the community is singularly heedless. It grants a pension, but shows no other sign of interest or respect. Often, of course, and oftener in the country than in the towns, relatives are attentive; and the common remark, that contact with the young keeps the old themselves young, supports the thesis here put forward. But too often relatives are indifferent, absent or non-existent, and sometimes the demands of their own children legitimately conflict with the claims of the old. It is little wonder that the old come to feel they are a burden on others, or, worse, that they are not needed and not wanted. This aggravates their sense of insecurity, against which their conservatism, their cherishing of every familiar link with the world of which they once formed a part, is a natural defence. If, on the other hand, they were to live in a circle of people who are interested in them and make reasonable demands upon them, who maintain with them the give and take of various personal relationships, it is likely that their mental horizon would narrow more slowly and their enterprise and adaptability last longer.

There is much still to be learned about the mentality of old age. A deliberate interest in studying it and observing its various patterns will do more than any teaching to help a doctor in the wise handling of the personal and domestic problems that arise. The aim, here stressed, of encouraging mental and physical activity, of helping even an old person to make the most of himself, will exercise the doctor's ingenuity. His understanding and tact will be needed to explain to younger members of families that the altering outlook or behaviour of old people is not to be resented or deplored but accepted as inevitable and treated with forbearance. It is of course in the "normal" old people and in those who have not reached the stage of overt degeneration that all this is most important. As degeneration proceeds treatment becomes increasingly a matter merely of providing physical care and protection, but still the best medicine demands an attitude of sympathy and helpfulness from those who attend. This is well reflected in the following description, unequalled in the text-books:

"We sometimes forget the intensely tragic nature of senile dementia.

It is so common we are habituated to it; so like a physiological process we take it for granted; as far as I know no sufferer has ever written championing it. On the contrary its usual reception is the mocking smile, the taunt-tinted phrase, the superior amused condescension, which make one feel that man has not advanced much beyond the fowls that pick at their sick one's sore. Cancer has its heroics, tubercle its melodrama, but the old lady fighting a stubborn rearguard action against senile dementia—cut off from help, her own side ashamed of her, fighting a low vegetative eating-away, not intoxicated as in the acute diseases but on the contrary with occasional moments of acute insight when she sees the battle in cruel

perspective, hopeless, helpless, ridiculous, intensely humiliated—only gets a jeer. It seemed so innocuous when it started—a lengthening of normal forgetfulness, an increase of ordinary hesitancy. Then ‘Where am I?’ or ‘What is to-day?’ or ‘What was I doing after breakfast, no, I mean, dinner?’ Later on it gets to be commented on by one’s dearest, who feel one’s humiliation so deeply: ‘Oh, but, my dear, I’ve told you a dozen times. . . .’ Enmity may come in here, the most revolting hate in the world because it is transmuted love. Then to cover up the more glaring lapses the old lady makes up fables to explain them. ‘I’m sorry to tell you, doctor, she’s becoming terribly untruthful, so unlike her.’ The old lady is fighting for more than life now, her place among the sane, and the fight goes on for years. One consolation she has, an old scrap-book of memories, but even here the pictures on the last pages are fading. Ordinary bodily needs are forgotten now, but sometimes realized; dirty clothes are hidden and poorly hidden. ‘Faulty habits,’ says the nurse; ‘secretive,’ writes the doctor. Then in one of her brief periods of perception she realizes how she is being treated as less than human and gets furious. ‘They’re after my money,’ ‘my house,’ ‘my cottage’ or even ‘my teapot.’ ‘Unmanageable,’ says the relative. ‘Give me my keys, I shall do my own shopping.’ ‘Violent at times,’ writes the alienist. She tries to explain, but although the intonation gives an idea of her feelings the words tumble into and over each other. She’s back to the stage of the animals who by growls or barking can convey their feelings but not precise information. It is the great primordial battle in reverse; once some speck of spirit that has grown to be ours fought its way into the animal world from the vegetable, now it is being driven back, fighting.” That account describes treatment in principle yet without mentioning it.

Finally, senile mental deterioration is often present in old men brought before the courts on criminal charges. It may be responsible for anything from petty stealing through sexual offences to homicide. Culpability depends on assessment of the mental state, for which a knowledge of the individual’s earlier mental condition and rate of deterioration is often necessary.

The following paragraphs discuss some aspects of the care of old people in the light of what has already been said. More detail will be found in recent books on “geriatrics.”

**Housing.**—Housing is perhaps the major problem in Britain to-day. The ideal is that husband and wife should grow old in a small house of their own, close to friends and acquaintances, and to relatives where possible, their social contacts continuing with both old and young. The planners of new housing estates would do well to provide accordingly. For widows, widowers and the unmarried, the happiest old age is often to be looked for in the homes of relatives of the next generation, and some share in the care of grandchildren is usually a great advantage; but overcrowding, or personal incompatibilities, can turn such proximity into a source of friction and distress. When old people live alone, from choice or from necessity, they suffer not only loneliness but the risk of going unattended in the event of accident or sudden illness. Old People’s Welfare Committees and other voluntary organizations in the larger towns have begun to take an interest in such people, arranging for them to be visited, to be helped in securing household necessities, and to be watched by their neighbours; someone who



will find out why an old woman's milk bottle is not taken in one morning may be in time to save her life.

Old People's Welfare Committees are also concerned to adapt new or converted houses as homes for the aged, especially for those who, though not ill, are no longer fully able to cook, clean and care for themselves. Much thought has been given to the size and staffing appropriate for these old people's homes. The aim is that they should be, in a worthy sense, homes and not merely institutions. Their scale of amenities will vary according to the resources of those who come to live in them and the amount of charitable or other endowment provided. It is sometimes possible to make them self-supporting, so far as running expenses are concerned, on the money available from the residents' old-age pensions, but their capital expenditure must be met in some other way. It is generally agreed that old people's homes should be small, not exceeding about thirty-six residents; that they should be situated near the homes of the relatives and friends of the residents, and reasonably near to churches, shops, cinemas, bowling greens, and the like; and that they should allow married couples to live together. They require staff in the ratio of one member of staff to every five residents or thereby. The task of the staff is not merely to administer, to provide meals, and carry out domestic work, but to befriend the residents individually and create an atmosphere in which they will be active within their limits, and happy. The old need both privacy and company; public rooms should be attractive and not large; single bedrooms, or, where that is not possible, rooms subdivided by cubicles or curtains, should give each a territory of his own and space for his possessions.

There are some obviously helpful amenities in the rooms or houses where old people live that are more easily provided in special homes but equally desirable where old people live independently or in family homes. They include a generous provision of warmth and light; avoidance of steep stairs and awkward steps; light chairs, not too low, easy to rise from or sit down in; low windows that can be seen through from a sitting position; baths with hand-rails; convenient hot-water supplies; indoor water-closets.

A Committee of the Nuffield Foundation, after an extensive survey of the problems of the care of old people, estimated that 5 per cent. of all houses in Britain should be suited to and available for the aged, including those living independently and those needing care in old people's homes. Several thousand more small homes are needed to accommodate healthy but enfeebled old persons now living apathetically in large institutions under restrictive rules and those no longer able fully to care for themselves yet not looked after by relatives. Large institutions, with internal subdivision and classification, are still required for those few among the enfeebled who are too difficult in behaviour or objectionable in habits to live with others in a home, and for those whose mental faculties have deteriorated.

As these varieties of accommodation for old people become increasingly available, and the demand for them grows, the doctor will often have to advise on what is most suitable for individual cases. In general, he will encourage old people to live independently, or with relatives, as long as possible, and will enlist the help of voluntary bodies or local authorities to improve their conditions of living. He will have to decide when independence, though still cherished, might better or must be sacrificed; as old people's homes become known to be something different from institutions,

it will be easier to persuade old people to enter them. When, from decline or disease, old people come to need continuous nursing care, they become patients, and should usually be cared for in hospitals, but there, in turn, home-like amenities should be provided to the extent that the patients are able to appreciate them.

**Work.**—In 1931 half the men of 65 and over, in England and Wales, were in paid employment; in Scotland more than half. The fraction is higher in agricultural communities, lower in industry. The old farm-servant goes on working as long as he can. The industrial employee is more likely to be discharged when he reaches pensionable age. Yet during the war, when men were scarce, some industrial areas employed from 54 to 88 per cent. of their men of 65 and over; in a mining area, where most of the work is arduous, the percentage remained as low as 25. From detailed enquiries of firms belonging to the Industrial Welfare Society, it appeared that they employed four times as many men of pensionable age as before the war. Of these, more than half retained their former jobs, especially if they had been skilled or clerical workers, and usually under standard conditions of hours and pay; fewer than half had been given different jobs, and only 15 per cent. had been given lighter work or shorter hours on account of their age. In general, elderly workers showed steadiness, reliability and unimpaired craftsmanship; they were slower than younger workers, less often absent, less successful with new machines or methods, and naturally less able for physically strenuous work.

These observations make it clear that old men can do a great deal of productive industrial work. That, it has been suggested above, is desirable both for the sake of their own health and for the welfare of the community. In a country where something approaching full employment is likely to be not merely socially advantageous but indeed a necessary means to economic survival, the retention of the old in industry becomes an important objective. The adjustments of wages and hours that may be required, the choosing of appropriate jobs, the avoidance of discontent among younger men who may feel their promotion delayed, and the distribution of age-groups fairly among competing employers, are all problems of industrial organization that lie mostly outside the medical field. Medicine, however, has two comments: first, that these problems must be solved, not shelved, or else both individual and social health will suffer; second, that men past 65 should be encouraged to work, willingly, on suitable tasks, but not forced to continue at work by economic or other pressure. The provision of the new National Insurance Act, whereby those who defer their retirement receive eventually a higher retirement pension, is in accord with this second principle.

Similar considerations apply to women, but on a much smaller scale so far as industry is concerned. For most, domestic work is their sheet anchor, and they should not be deprived of it except for good reason. The zeal of devoted children and grandchildren to spare them effort may do them harm, and the doctor, watching the routine of a household of mixed ages, may sometimes find it wise to suggest that the grandmother be given a greater share in the work and responsibility of the home.

For those no longer employed, especially if they live alone or in old people's homes, there remains the possibility that handicrafts may afford not only interesting but actually useful and productive occupation. This

has yet to be fully explored. First attempts to engage old people in handicrafts new to them are apt to meet with resistance, but with skilled instruction and encouragement surprising successes have been achieved.

Among business and professional men the management of retirement is as difficult as with manual workers. The same biological principles apply, but are not applied; namely, that the amount of work or responsibility undertaken by an ageing man should be progressively decreased in proportion to the decline of his strength but not faster, and that the work or responsibility should be of a kind which he can carry with satisfaction to himself and to others. Compulsory retirement at a fixed age is a crude and wasteful device, small improvement on the system it replaced, wherein the holder of an office was allowed, and at times to earn his bread was obliged, to retain the office till he died. Compulsory retirement can be justified only if it is accompanied by the provision of alternative appointments, part-time or less arduous, open without too great sacrifice of prestige to those who retire from responsible positions. Compulsory retirement, on the other hand, is a safeguard against the aggregation of power and responsibility in the hands of those who are old. In a stable or static society securely based on agriculture, this aggregation is no bad thing; with age comes wisdom, and the old retain for a long time their soundness of judgment—in situations whose pattern is familiar. But in new and changing situations they are less adaptable than the young and the middle-aged, and it follows that in a rapidly changing industrial society facing new stresses, old men should not predominate in positions of leadership and responsibility. It would seem dangerous to abolish compulsory retirement or to raise the age limits without careful scrutiny. Clearly it is an urgent problem for the several professions, for those concerned in government, and for those in control of industry and commerce, to overhaul their methods of making and ending appointments, in a biologically-minded way. In general, the amount and the kind of effort demanded of men should be separately suited to their waxing or waning capacities at different ages; yet, while the average demand should match the average resources, the system must be so elastic as to give relief to the man who ages quickly and—of great importance—opportunity to the rare and valuable person who remains mentally younger than his years. Medical advice is needed in facing the social problem; and, whatever society's arrangements may be, medical advice will often be needed by the individual faced with the choice of retiring, not retiring or in some way curtailing his activities.

**Other Interests and Activities.**—During leisure, the need of the old for health-giving physical and mental activity is to be met by hobbies, games, gardening, reading, social intercourse and religious fellowship. The cinema and the wireless contribute. Those who had time and energy for these things during their active life will more easily continue them into old age and benefit thereby. Those whose earlier opportunities were limited, or who lived entirely for their work, are reluctant to take up activities new to them in their retirement; they are apt to become apathetic, or self-centred and querulous. Yet there is evidence that skilful persuasion, backed by a genuine and friendly personal interest, will often engage hesitant old people in one or other of these interests, with great advantage to themselves. The task falls to relatives, friends, Old People's Welfare Committees and the organizers of old people's homes and clubs; the doctor suggests or advises,

watching how far it proves possible to foster activity in the old without detriment to their peace.

**Diet.**—"Most old people over-eat" is the surprising dictum of certain wardens of old people's homes. Many observers think otherwise. Poverty and rationing restrictions, the latter bearing exceptionally hard on old people living alone, lead to undernutrition. Imperfect teeth and lack of dentures limit many old people to soft foods. Failing taste and smell lead to lessened appetite. Cooking and preparing food for one or two people only grows tedious and is neglected. Inadequate and ill-balanced diets are probably much more common than excessive ones.

Yet "the competence of healthy older people is largely a matter of nutrition." The diet to be aimed at should no doubt be less in caloric value than that of an active adult—since both basal requirements and the amount of activity are lessened in age; but it should not fall below 1,500 calories for women and 1,800 calories for men of average size. It should contain 0.75 to 1 gm. per kilogram of protein, and should not eschew meat. Potatoes, vegetables and fruit are as necessary for their vitamin and mineral content as in younger persons; where chewing is inadequate they may have to take the form of purées and fruit juices. Milk and especially cheese are valuable for their calcium content; it has been thought that the broken femoral necks in old people are a consequence of years of inadequate calcium intake. Fried and fatty foods are apt to be ill tolerated and should be restricted. Tea and coffee do more good than harm, and the same is probably true of small amounts of alcohol. In healthy old age eating and drinking should continue to be a source of lively satisfaction, and those who cater for old people should try to make them so. Food and drink exhilarate as does nothing else. Yet the eating habits of old people are difficult to change, and much patience and persuasion may be needed to convert a lonely old woman, who has been living on her meat ration, bread, butter or margarine, tea and jam, to an adequate and varied diet; but where such people, entering old people's homes, have learned to eat well, a marked improvement in their general health and outlook has been observed. Sometimes concessions to taste or prejudice have to be made. In the minority who over-eat, obesity should be checked by appropriate limitation of fat and carbohydrate.

**General Physical Care.**—A first concern is to provide those who need them with adequate spectacles, adequate teeth and hearing aids. Dentures may be difficult or even impossible to wear in mouths that have long been nearly edentulous, owing to thinness of the atrophic mucous membrane; it is sometimes better that a person in the fifties or sixties should part early with remaining teeth and begin wearing dentures while the mouth is robust.

Deafness is very common in the old, and can isolate them cruelly. There should be a wide extension of the use of modern hearing-aids and an effort to persuade the old to use them with no more reluctance than they feel towards glasses. Their use needs to be learned.

Sleep habits and sleep requirements may change in old age. Some old people seem to need a longer night in bed. Many waken early in the morning and complain of insomnia, which is more apparent than real. Very many old people benefit from one or more short sleeps during the day, either in bed or in the less relaxing posture of sitting in a chair. The routine of their day, especially if they live in homes, should take this into account.

Baths for old people should be warm but not hot. When the physical effort they involve comes to be a burden they need not be too frequent: once or twice a week should suffice for cleanliness.

The old usually wear more and warmer clothing, some to excess. Indoors, at least, the aim should be sufficient warmth in the environment to avoid the need for too many clothes, which restrict movement. Most old people, if encouraged, will take some pride in their clothes and their appearance, and with benefit—a point to be remembered in old people's homes, where uniform clothing should always be avoided. The advantage of moderate exercise is obvious.

Tobacco affords great comfort to the old. The only medical grounds for its restriction are amblyopia, a demonstrable effect in producing cardiac symptoms or pharyngitis, and peripheral vascular disease.

The care of the feet, described on p. 375 as suitable for diabetics, is appropriate for all old people.

Constipation has the same causes in old age as in younger people, but the re-education of a bowel that has long been habitually constipated may be no longer possible. Regular doses of cascara, senna or aloin then come to be justifiable (see p. 563).

The response to drugs in old people probably shows as much variation from individual to individual as in the young. Any regular differences due to age are therefore difficult to recognize. We know of no controlled observations on the subject, but clinical experience suggests some generalizations, for example, that opiates have a more powerful effect in the aged. The wider generalization is perhaps that in old age stimulants are less stimulating and depressants are more depressing. This may afford some guide to dosage, which, however, will remain, as in the therapeutics of younger persons, essentially a matter of trial and error.

**Illness in Old People.**—The common illnesses are the degenerative ones, especially those of heart and nervous system, that result from impoverished blood supply. The infections to which old age is subject are chiefly those of the respiratory tract—acute and chronic bronchitis, pneumonia and tuberculosis. Injury is common. Malignant disease has its highest absolute incidence in the decade 65 to 75, but the proportion of persons living who develop cancer goes on increasing after 75 and through the eighties.

In old age the constitutional response to infection is less vigorous than in younger persons. The onset of illness is more insidious and may attract little attention. Pneumonia, for example, may run its course with no rise in pulse-rate or in temperature and only an acceleration of breathing. Malignant disease too may begin and advance more unobtrusively in the aged. Recovery from acute illnesses and operations, and the repair of fractures and other injuries, are slower in the old. Yet, paradoxically, this does not call for more prolonged rest in bed, but only for a more gradual return to full activity. Immobilization of an old person involves the risk of hypostatic pneumonia, of venous thrombosis, of bedsores, and of an irreversible stiffening of the limbs and weakening of the muscles. While in bed an old person should be moved from one position to another every hour or two, and persuaded to move his arms and legs (the latter being always protected by a bed-cage) frequently. This active movement, which may be systematized in the form of remedial exercises, should begin as early as possible in convalescence, preferably within the first week, not only from

operations and infections, but also from such episodes as coronary thrombosis and cerebral thrombosis. As early as returning strength will allow, the patient should be moved into a sitting position in a chair for short periods. Indeed, it is not unreasonable to nurse an old patient sitting in a chair through the whole course of an attack of pneumonia. Whenever possible, bedpans should be avoided, a bedside commode being used instead. The possibility that constipation may lead to fœcal impaction should be kept in mind.

Old people stand surgical operations surprisingly well. If an operation is urgently called for to relieve severe pain or to save life, and the patient's fitness to survive it is in doubt, the risk should usually be taken. If the operation is one that is expected rather to prolong a life not immediately threatened, an attempt must be made to compare the patient's expectation of life if no operation is performed with his expectation of life after a successful operation; these estimates, with allowance for the operative risk, guide the decision. Thus an operation for malignant disease, carrying a high operative mortality, may be justified in a patient of 70, but not in one of 80, who, with or without the carcinoma, has few years to live.

In chronic illness, such as hemiplegia, arthritis or protracted heart failure, the chief requirement is faithful nursing. Patients who retain their mental faculties should be segregated from those who have so deteriorated as to become unpleasant or dirty companions. In addition to food, warmth and mechanical care, the mentally capable need personal interest, occupation and encouragement to activity both in and out of bed. Without these they pull the sheets over their heads and vegetate, but with enterprising management a wardful of aged chronic sick can become a cheerful place. Even incontinence diminishes.

**Summary.**—It will be clear that the care of old people is a social as well as an individual problem. Likewise the study of their needs and their potentialities is a task both for social medicine and for individual medicine. The aim of both should be "to add life to years rather than years to life."

R. S. AITKEN.

# INDUSTRIAL DISEASES

## INTRODUCTION

"When a Handicrafts-man is taken ill, he must be cur'd by Vomiting, or Purging, or Searing, or Incision; for if a Physician tells him of a long Diet, and Bolstering up his Head, and the like, he presently replies, That he has not leisure to lie by it, and that it will be of no use to him to lead an idle crazy Life, and neglect his Business. Upon this he takes leave of the Physician, and returns to his usual way of living."—PLATO, quoted by RAMAZZINI (1705).

THE difficulties that beset the physician of Plato's Republic in the treatment of the diseases of tradesmen have persisted through the ages. Industrial disease is usually well established before advice is sought, and often, as in silicosis, progressive in nature; the patient's financial resources are small and his family anxieties correspondingly great, while he is faced with eventual return to work that has been responsible for, or has contributed to, his illness. All these factors operate against the prospect of cure: as Ramazzini himself wrote of the diseases of potters:—

"... 'tis a hard matter to light upon such Remedies as will restore them to perfect Health: For they seldom have recourse to the Physicians, till the use of their Limbs is taken from 'em, and their *Viscera* grown hard; besides, they are commonly pinch'd with another Evil, viz., Extream Poverty."

In relation to industrial disease, prevention and treatment must essentially go hand in hand and it may be helpful to summarize the broad aims of prevention in this field.

1. The provision of properly adapted buildings, with facilities for keeping the workshops clean, and for effective ventilation.
2. Apparatus designed for its special purpose.
3. Appliances for the arrest of dust and gases at their place of origin and for their adequate removal and disposal.
4. So far as possible, avoidance of direct contact with poisonous materials: utmost possible reduction in hours of labour in dangerous employments.
5. Displacement of particularly dangerous methods and materials and the substitution of less dangerous materials.
6. Instruction of new workmen in the risks inherent in their work.
7. Constant supervision of all dangerous employments by expert and responsible persons.
8. Employment of appropriate means for personal protection—suitable work clothes, caps, goggles, etc.
9. Practice of personal cleanliness by workers concerned, and their utilization of facilities provided.
10. Immediate report of symptoms of illness and early attention to all injuries, however slight.
11. Employment of working personnel physically and mentally fit for the job, with, where necessary, periodic medical examinations and alternation of employment.

Some of these postulates, like measures for dust control, are essentially mechanical; some involve substitution of toxic agents by others less harmful, as in the classical replacement of yellow phosphorus in the manufacture

of matches; while others involve close and continuing medical supervision in such matters as selection of personnel for particular work, alternation of employment, and painstaking search for the beginnings of disease. A great deal has been accomplished in Britain since the beginning of the present century towards the improvement of working conditions, mainly through the efforts of the Factory Department. The Factories Act (1937) makes possible yet further advances, notably perhaps by making more effective the medical supervision of young persons entering industry. A summary of the principal changes effected by this important piece of legislation may be obtained—like other official publications on industrial health—from H.M. Stationery Offices.

But, while industrial disease may conform to the clinical picture of a classical trade intoxication, certain classes of workmen suffer rather from an excessive incidence of incapacitating sickness of a type not peculiar to a specific occupation. The excessive sickness falls chiefly into certain groups (injuries, rheumatic conditions, gastritis and dermatitis, for instance, in the case of coal-miners) and its association with employment, though real enough, is not always appreciated. Even unemployment, with its curious sequence of psychological changes, clearly influences health; while re-employment has problems of its own, such as increased liability to injury to the back and sepsis of the hands during the period of hardening.

Many factors quite outside the scope of factory control may influence the susceptibility of workers to industrial disease, and there is need for increasingly close co-operation between general practitioners and their professional colleagues charged with the more technical supervision of health conditions inside the factory. It cannot be too clearly recognized that the health of industrial workers is governed by the sum of working conditions within the factory and of living conditions (housing, etc.) outside, and that improvement of the health of an industrial community should be approached along both these lines, a fact recognized in this country by the Miners' Welfare Commission. Under the compelling stimulus of war conditions more intensive care has been given to the health of workers, especially those engaged in the production of munitions. It is worthy of note that increasing numbers of industrial concerns have set up within their factories health organizations under the charge of a medical officer who is anxious to co-operate with outside practitioners in safeguarding the health of workers.

Another way in which the practitioner can further the prevention of industrial disease is by immediate compliance with his statutory duty to notify to the Chief Inspector of Factories, Ministry of Labour and National Service, London, all patients whom he believes to be suffering from the prescribed diseases (anthrax, toxic jaundice, toxic anæmia, compressed air sickness, epitheliomatous and chrome ulceration; and poisoning by lead, arsenic, phosphorus, mercury, manganese, carbon bisulphide, aniline and benzol) contracted in the course of employment. The condition "toxic anæmia," recently added to the list, "is intended to apply to dyshæmopoietic anæmia occurring in a person employed in a process which brings him into contact with X-rays, radio-active substances and any chemical compound which may be capable of causing this effect."

Apart altogether from exposure to toxic substances some occupations demand from the operatives unusually severe physiological response. Some, like iron moulding and certain kinds of labouring, must always call for



heavy muscular effort, while it has been found necessary to control by law the weights that may be lifted by women and children.

## EFFECTS OF HIGH TEMPERATURES

Other kinds of work expose operatives to the effects of high temperatures. Over a hundred years ago Thackrah recommended "for such as work at high temperatures" (1) diminution of muscular labour performed in hot rooms; (2) the drinking of lemonade, or other diluent during the time of labour, rather than the noxious compound called ale; (3) the use of stimulants with the food after labour; (4) the reduction of the period of labour.

Heat disease may be classified into three clinical types: (1) Heat cramps; (2) heat exhaustion; and (3) heat retention.

**Heat Cramps.**—For the prevention of heat cramps saline waters (0.10 to 0.20 per cent.) chilled to a temperature of 45° to 50° F. should be made available to the workers: 5 gm. of salt added to a gallon of water is adequate to prevent heat cramps and is not unpleasant to drink. In the treatment of severe heat cramp intravenous injection of saline solution is invaluable.

**Heat Exhaustion.**—For prevention of heat exhaustion "jelly drops" containing approximately equal parts of glucose and granulated sugar are commonly used in America, while in this country many workers carry to work sweetened lemonade, which is useful both for maintaining blood-sugar level and for preventing acidosis. In the treatment of heat exhaustion the administration of glucose should be combined with sodium bicarbonate.

**Heat Retention.**—For the treatment of heat retention the essentials are (1) immediate reduction of the fever; (2) rest in the recumbent posture; and (3) administration of fluids. The patient should be removed to cool surroundings, his head elevated, cool water sprayed over the body with, if possible, fans placed to evaporate the water, and cutaneous circulation maintained by gentle friction. Fluids should be given in abundance, orally, intravenously or subcutaneously, for it is important to secure rapid restoration of circulating fluid volume; 500 c.c. of plasma may be given intravenously, and repeated in forty minutes if blood-pressure response is not satisfactory. Artificial respiration may be necessary where there is respiratory failure: and to combat tissue oxygen deficiency oxygen may be administered by mask. Adrenaline may be required to counter cardiac insufficiency, though it should be used only if strictly necessary because of its tendency to produce petechial hæmorrhage in these cases. Rest in bed should be prolonged, and the patient's subsequent work carefully supervised: convalescence is often slow.

This drink has been found useful during hot weather by workers exposed to high temperatures:—

Sodium chloride . . . . .	6 oz. (0.18 kg.)
Potassium chloride . . . . .	4 oz. (0.12 kg.)
Water . . . . .	1½ pints (1 litre)

Seventeen fluid ounces (0.48 litres) of this concentrated solution to be added to 3 gals. (13.5 litres) of water for drinking: a flavouring agent may be added if required.

The drink can be made more palatable by modification as under:—

Sodium chloride . . . . .	1 lb. (0.45 kg.)
Potassium chloride . . . . .	10½ oz. (0.33 kg.)
Citric acid . . . . .	5½ oz. (0.17 kg.)
Saccharin . . . . .	3 gm.
Oil of lemon . . . . .	22 c.c.
"Lemon squash" colouring . . . . .	A small quantity
Water . . . . .	to 3 litres

Add 1 part of this concentrated solution to  
30 parts of water.

Tablets containing similar ingredients are now available for the ready preparation of palatable saline drinks.

## WORK IN UNUSUAL ATMOSPHERIC PRESSURES

**Compressed Air.**—Another type of strain on physiological adaptation is that involved by work in compressed air. Among the precautions taken to prevent compressed air illness are (1) medical supervision by physicians with experience of work entailing the use of compressed air; (2) preliminary medical examination of personnel; (3) limitation of hours of work in compressed air; (4) slow decompression, with rigid adherence to a prescribed technique; and (5) provision of a hospital lock for dealing with cases of caisson sickness. In selecting workmen the essentials are normal lungs, normal kidneys, and a good heart; blood pressure should not be above normal. According to Singstad many American States have codes of regulations which require supervision by a qualified physician experienced in work with compressed air to secure (a) examination of each new worker; (b) test of each new man under actual working conditions; (c) re-examination of any worker absent from work for ten days or more; (d) periodic re-examination of all workers; (e) prohibition of employment of alcoholics; (f) complete record of all examinations and illnesses; (g) a medical lock 5 to 6 ft. in diameter, with a physician in constant attendance when pressures exceed 17 lb. per sq. in. Adequate dressing-room facilities should be provided and hot coffee should be served to workers on their return from the air chamber.

In Britain the Committee on Regulations for Work carried out in Compressed Air recommended in 1936 that after 25 to 40 lb. pressure men should be kept for forty minutes after decompression before leaving the works, and that with 40 to 50 lb. pressure they should be kept for one hour.

Recompression and slow decompression is the recognized treatment of compressed air illness. It should be used as soon as possible after the onset of the illness. Recently the American Naval Medical Research Institute has reported great success from the use of a standard technique which includes three basic principles: (a) limitation of recompression to a maximal pressure of 65 lb. per square inch, maintained for from 30 to 120 minutes; (b) more prolonged recompression for periods of 12 to 24 hours at pressures equal to depths between 30 and 60 feet; and (c) inhalation of oxygen to promote more rapid elimination of nitrogen.

Helium oxygen mixtures have been suggested for the treatment and

prophylaxis of compressed air illness almost since the time of recognition of the properties of helium. In the treatment of tubal and sinus block and aero-otitis the nose is sprayed with a 2 per cent. solution of ephedrine sulphate preparatory to the administration of helium. This gas is given in a mixture consisting of eighty parts of helium and twenty of oxygen under positive pressure. The apparatus consists of a mask, a breathing tube, a spirometric breathing bag, a calibrated valve and weights for producing pressure in the system. The positive pressure can be regulated from 6 mm. to 32 mm. of mercury. The average patient obtains relief in four minutes at a rate of flow of 8 litres per minute and a pressure of 12 mm. of mercury. Obstinate cases may require ten minutes; longer treatment is useless. It has been found that treatment with helium reduces the number of days lost from work and decreases the incidence of suppurative otitis media.

**High Altitudes.**—In flying at high altitudes anoxia is caused by decreased partial pressure of oxygen in the inspired air. Factors other than altitude influence the onset of symptoms, notably the rate of ascent.

The minimization of these ill-effects lies largely in the proper selection of pilots. This involves thorough medical and laboratory overhaul, with special investigation of the eye, ear, nose and throat and of nervous and psychological suitability. Re-examination of pilots should be carried out regularly. Pilots who have been too long in service are apt to become mentally and physically tired. If complete rest is impossible the hours of flying, particularly of flying at night and in bad weather, must be reduced. In any case protection must be afforded against wind, noise, cold, vibration, glare and noxious gases.

## WORK WITH PNEUMATIC DRILLS

Though there is no effective method of preventing the functional nervous disturbance so frequently associated with the use of pneumatic drills, efforts have been made to minimize another trying disability of these workers—that associated with changes in the bones and joints and a pronounced vaso-constrictive effect leading to attacks of blanching and numbness in the fingers, with loss of power, usually affecting the left hand. By way of prevention, it is recommended that work of this kind should not be continued for more than one year. Attempts have been made to prevent this condition by wearing protective resilient pads, though with indifferent success; and treatment of the spasmodic vaso-constriction by histamine ionization to the affected hands has been tried, but the avoidance of cold, perhaps the most useful therapeutic advice, often presents great difficulty under British climatic conditions.

## MINERS' NYSTAGMUS

Though there has been in the past a good deal of difference of opinion about the relative importance of faulty illumination and psychological disturbance in the production of miners' nystagmus, there is now fairly general agreement with the observations on prevention and treatment in the Reports of the Miners' Nystagmus Committee of the Medical Research Council published in 1922 and 1932. The Reports insist on the importance of adequate treatment.

"Although it is of fundamental importance that every effort should be made to improve the lighting of mines . . . yet it is also of the utmost importance that the psychological aspects, not only of this disability but of similar conditions in other occupations, should be fully recognized.

*"The Committee are strongly of opinion that the practical treatment of the disease from an administrative point of view should consist in the elimination of a hopeless dependence on compensation by the provision of opportunities for work of some kind, the end in view being complete restoration to full work underground, under conditions of proper illumination, even if this has to be preceded by a period of work in daylight."*

More recently a Departmental Committee has reported along similar lines. It recommends that to improve lighting in mines the electric cap lamp should be given wider use; cases of nystagmus should not be certified unless oscillations have been present for a definite period, and Medical Boards should be set up in the coal districts to advise on all phases of the subject. As work plays a very important part in recovery and in preventing psycho-neurosis, each sufferer must be given a job and employers should co-operate in finding such work.

In their evidence to this Committee the British Medical Association classified wholly incapacitated cases into (a) those likely eventually to resume their previous work (generally they should not be idle more than six months), and (b) those unsuited for the industry, though many are fit for training in vocational centres, especially if they have developed nystagmus within five years after becoming miners.

"In the early stages change of work to other parts of the pit will often put off a threatened attack. If the symptoms continue the man should be put to work on the surface. Rest from underground work and surface employment are the only specifics for nystagmus, and medical treatment except that directed to the general health of the patient is of little avail."

Various symptomatic measures have been advocated, but the results have been indefinite. Any refractive error should be corrected.

## POISONING BY METALS

**Lead.**—The number of reported cases of lead poisoning has fallen enormously during the present century. Numerous preventive measures have contributed to this reduction. Innocuous materials have been substituted for those containing lead (as in paints and low solubility glazes). Steps have been taken for the control of lead-laden dust, the precise measures varying with the individual requirements of the industries concerned. The employment of women and young persons in certain processes involving the use of lead has been prohibited, and general hygienic measures have been introduced to minimize the risk of poisoning—for instance, prohibition of taking meals in workrooms and the introduction of adequate washing and dining facilities, together with strict insistence on the importance of personal hygiene.

Periodic medical examination by the Examining Surgeon (or other medical man appointed by the Chief Inspector of Factories) is required at intervals ranging from weekly (in the manufacture of compounds of lead) to quarterly (as in vitreous enamelling), the frequency varying with the risk

involved. In carrying out these periodic medical examinations special attention should be given to a survey of the general health and to a search for early evidence of extensor paralysis. Lane has demonstrated the value of systematic blood examinations in the control of lead poisoning in industry; he believes that in general an increase in the degree of punctation of the red blood cells among workers exposed to lead indicates an increased risk.

A considerable number of cases of lead poisoning now occur as a result of the inhalation of lead vapour in the course of ship-breaking by the use of oxy-acetylene. In this occupation preventive measures are difficult to apply and the clinical picture is more acute than that usually experienced in other forms of industrial lead poisoning. Periodic clinical examination has proved to be of little value in anticipating the onset of symptoms, but it has been demonstrated that systematic examination of blood films, at intervals not greater than one week, in conjunction with clinical examination can be of real assistance. With inhalation of lead-laden fume there is a rapid pouring out of red blood cells showing punctate basophilia in stained films and of large immature lymphoid cells; so long as the workman is able to respond in this way to the inhalation of lead, he does not appear to be in imminent danger of poisoning. As the vigour of his defensive reaction diminishes in the presence of continued exposure to lead fume, fewer punctate cells and immature lymphocytes are to be found in the circulatory blood, and clinical signs of poisoning are liable to appear: so that a fall in the ratio of punctate cells or of large to small lymphoid cells is to be regarded as a danger signal calling for a reduction in exposure to lead. A high degree of punctation may be found in these cases following a transfer to a minor risk, while punctate basophilia may be minimal in the presence of severe toxic symptoms.

It has long been the custom to encourage workers in lead industries to take drinks believed to be of service in the prevention of lead poisoning. Sulphuric acid orangeade is regarded as one of the best:—

Dilute sulphuric acid . . . . .	12 parts.
Concentrated infusion of orange . . . . .	12 parts.
Syrup of orange . . . . .	40 parts.
Water . . . . .	16 parts.

One part to be added to 32 parts of water. Daily dose, 3 oz. (85.2 c.c.).

Recent work indicates that good results may be obtained in the prevention of lead poisoning, and during the treatment of the acute stage of the disease, by the administration of 100 to 200 mg. of vitamin C daily for several weeks.

The treatment of lead poisoning falls into two stages, first immobilization of the circulating lead, and later its elimination. It is believed that there is a close relationship between calcium metabolism and the behaviour of lead in the body. Lead can be immobilized in the bones by the administration of calcium given in large doses, either as 30 gr. (1.8 gm.) of calcium lactate by the mouth three times a day or as calcium gluconate (10 c.c. daily of a 10 per cent. solution intramuscularly), supplemented by a diet rich in calcium (milk); and this immobilization relieves acute symptoms dramatically.

Deleading of the patient should be undertaken only after the acute symptoms have subsided and under the most careful clinical observation,

with repeated blood examinations. To promote excretion of lead a low calcium diet (reduced intake of milk, cheese, egg yolk and green vegetables) is combined with the administration of dilute acid or 20 gr. (1.2 gm.) of ammonium chloride three times a day. The effect of these can often be enhanced by the administration of parathyroid extract (50 units daily), but it must be used with care, as acute lead poisoning has been produced by undue haste in deleading.

Sodium bicarbonate and potassium iodide have been used to mobilize stored lead, but both are liable to provoke symptoms of lead intoxication, particularly sodium bicarbonate.

Symptoms may call for palliative treatment, colic for an enema, hot application to the abdomen or even morphine. Goadby recommended for colic the administration of gr. i (0.06 gm.) of sodium nitrite or 2 minims (0.12 c.c.) of liquor trinitrini, as in addition to the spasm of the intestine there is considerable vaso-constriction of all the vessels in the mesenteric area. Magnesium sulphate is useful in the treatment of constipation.

Splinting, massage and electricity, notably galvanism, have been found to be serviceable in the treatment of lead paralysis.

For the treatment of anæmia see p. 461.

**Arsenic.**—Cases of poisoning by arsenical salts are nowadays rarely seen in industry. The general preventive measures that have been found most useful are substantially the same as those for the prevention of lead poisoning. The prevention of poisoning by arseniuretted hydrogen implies a knowledge of the extent of arsenical contamination of materials used in industry and recognition of the danger of this poisoning. Operations liable to produce arseniuretted hydrogen should be carried out only in closed apparatus or under good artificial exhaust ventilation. Strips of mercury bromide paper, which show by a yellow colour small traces of arseniuretted hydrogen, should be hung in the workrooms. In the face of a known risk of poisoning by arseniuretted hydrogen, it is a good plan to secure regular daily examination of the urine for the presence of blood.

In the treatment of acute poisoning by arseniuretted hydrogen the first essential is the administration of oxygen. Blood transfusion may be necessary. Convalescence is always slow and calls for prolonged care of the general health.

The treatment of chronic arsenical poisoning consists in removal from exposure and in promoting elimination through kidneys and bowels. Sodium thiosulphate orally in 15 gr. (1 gm.) doses, or preferably intravenously in 10 per cent. solution, increases the elimination of arsenic. For the treatment of peripheral neuritis (here as with other poisons) 10 mg. of vitamin B<sub>1</sub> daily have proved valuable, improvement being noticeable in a few days; cases so treated are not so liable as others to severe diarrhoea.

In the treatment of severe cases of arsenical poisoning B.A.L., developed during the war as an antidote to the arsenical blister gases, has been found useful: 3 mg. of B.A.L. (10 per cent. in oil) per kilogram of body-weight should be given intramuscularly every four hours for the first two days, 4 injections on the third day, and injections twice daily thereafter for ten days or until complete recovery. For milder cases smaller and less frequent injections may suffice; but successful treatment by B.A.L. of arsenic (or mercury) poisoning depends on early institution of treatment and on the use of adequate amounts of B.A.L. at frequent intervals. Other

supportive measures should always be used in conjunction with B.A.L. therapy.

**Mercury.**—Mercury poisoning has long had a direct interest for the medical profession. As long ago as 1705 Ramazzini wrote:—

“Now a-Days, those who rub the Mercurial Ointments on Pocky Persons, are the meaner sort of Surgeons who undertake that Office to make a Penny by it; for the better sort of Surgeons decline such a sordid Piece of Service, which is likewise accompany’d with Danger.”

By that time even the meaner sort of surgeons had learned to let their patients do their own rubbing:—

“But if such Surgeons have contracted any Harm by the Inunction, such as the Shaking of the Hands, a Giddyness in the Head, and Gripings of the Guts; in this Case, as I said before, the Decoction of *Guaiaicum* is the Remedy.”

The preventive measures applicable to mercurialism in Ramazzini’s time included the consumption of fat broth and generous wine: by the time of Thackrah (1833) they were more prosaic—personal cleanliness, change of dress and attention to ventilation, measures which are still commonly used.

It is important to secure limitation of the area of mercury exposed to the air and as low a temperature in the workroom as possible, since volatilization increases rapidly with temperature. Floors and work benches should be smooth and impervious and should drain to a collecting trough. All vessels containing mercury should be kept covered.

Frequent attention to the teeth is desirable: they should be examined regularly and necessary dental treatment undertaken. Regular brushing is important, and the use of a mouthwash, *e.g.*, hydrogen peroxide, or that recommended by Legge:—

Alum.	.	.	.	.	.	gr. v (0.3 gm.)
Pot. Chloras.	.	.	.	.	.	gr. v (0.3 gm.)
Glycer.	.	.	.	.	.	fl. dr. $\frac{1}{2}$ (1.8 c.c.)
Aq.	.	.	.	.	to	fl. oz. i (28.4 c.c.)

For the prevention of ulcers from exposure to fulminate of mercury the use of a 10 per cent. solution of sodium hyposulphite has been recommended as a local application.

In the selection of workers there should be excluded those suffering from tuberculosis and nephritis, and those of inferior physique, as well as women and young persons.

The actual treatment of mercurial poisoning consists largely in removing the patient from exposure to mercury, in attention to his general health and in promoting elimination by bowels and kidneys. Many medicines have been tried. Thackrah reported a hundred years ago that he found opium the most efficient remedy for the salivation from which most patients suffer; for the tremors he recommended rest, fresh air and aperients.

As in poisoning from arsenic, B.A.L. has been found useful in the treatment of mercury poisoning, but here larger doses of B.A.L. are found to be necessary, an initial dose of 5 mg. per kilogram being followed in two hours by a dose of 2.5 mg. per kilogram. After a lapse of 2 to 4 hours another dose of 2.5 mg. per kilogram should be given, and in patients with severe poisoning a third similar dose should be given within the first 12 hours of therapy.

In the treatment of conjunctivitis caused by fulminate of mercury Legge recommended the use of a 2 per cent. solution of sodium hyposulphite as an eyewash.

**Selenium.**—Selenium is being increasingly used in industry: it affects chiefly the liver (with atrophy and cellular destruction mainly around the central vein), kidney, blood (with primary increase in hæmoglobin followed by distinct decrease) and the skin.

Prevention follows lines already described; in addition, the wearing of a simple gauze mask has been found useful in preventing the collection of dust in upper nasal passages (catarrh; expistaxis). All operatives complaining of vague symptoms should be carefully examined, with hæmoglobin estimation and a test for urinary selenium in a 24-hours' specimen. The administration of 3 minims (0.2 c.c.) of bromobenzene three times a day after meals for short periods not exceeding five days will render labile selenium fixed in the tissues so that it is excreted in the urine.

#### B.A.L. (BRITISH ANTI-LEWISITE) IN THE TREATMENT OF POISONING BY SOME HEAVY METALS

B.A.L. (2, 3-dimercaptopropanol) was developed secretly during the war, jointly in Britain and in the United States, to counteract the toxic effects of arsenical gases such as Lewisite which might be used by the enemy. It was, fortunately, never required for this purpose but, in peace-time, as stated above, has provided us with an important therapeutic weapon, sometimes life-saving in its effects.

It is satisfactory to note that the discovery of B.A.L. followed a definite line of research and confirmed an interesting hypothesis, namely, that arsenic acts as a poison by combining with and inactivating sulphhydryl groups in the enzymes of proteins. A drug was sought which would compete effectively with these enzymes for the arsenic and form a non-toxic arsenical compound, rapidly excreted. The result of the research was B.A.L., which, if given soon enough, rapidly binds the arsenic and renders it inert.

The heavy metal against which B.A.L. was primarily directed was arsenic, but since then its value has been proved in poisoning by mercury (see above) and recent evidence suggests that it may also be effective in the complications of gold therapy in rheumatoid arthritis (p. 812). It has been tested also with other metallic poisons, and in one, cadmium, the compound formed is definitely injurious to the kidneys. The uses of B.A.L. are therefore at present limited to combating the toxic effects of arsenic, mercury and possibly gold.

In the earlier work, especially on arsenical poisoning, B.A.L. was administered both by injection and by inunction, but the former alone is now recommended. At present B.A.L. is used in the United States as a 10 per cent. solution of the drug in peanut oil with 20 per cent. benzyl benzoate added. In Britain, ampoules made up similarly but containing only 5 per cent. of B.A.L. have so far been employed.

Various side-effects following the administration of B.A.L. have been observed, which include nausea, vomiting, a burning sensation in the mouth, throat and eyes, pain in the teeth, lachrymation, salivation and elevation of the blood pressure. They generally occur rapidly, within 15 to 20 minutes after each injection, and are all of a temporary nature.



## POISONOUS FUMES AND GASES

Henderson and Haggard illustrate the general type of precaution needed to prevent atmospheric contamination by noxious fumes and gases from industrial processes by reference to the rules applicable to an ammonia refrigerating plant.

1. The refrigerating equipment including valves and piping should be inspected at frequent and regular intervals, and suitable repairs made immediately when needed.

2. Every employee should be instructed regarding the dangers from ammonia and trained to avoid them.

3. No one should be allowed to sleep in rooms adjoining a refrigerating plant.

4. The rooms in which machinery is installed should have doors opening directly to the outside air. The position of these rooms should be such that escaping fumes cannot invade other parts of the factory or cut off the escape of persons in them. Regulations should be strictly enforced requiring that exits shall never be obstructed by temporary scaffolding or other impediments to escape.

5. Gas masks with canisters affording protection against ammonia should be provided. They should be stored in some locality readily accessible to, but outside the rooms in which there is a possibility of the escape of ammonia.

6. Every workman engaged in repair work on refrigerating apparatus should be required to carry a gas mask strapped to his body or hung round his neck in anticipation of the possible escape of ammonia.

7. A valve arranged to shut off the ammonia at the storage cylinders should be placed where it can be manipulated from the outside of the building.

Noxious gases encountered in industry may be classified according to their physiological action:—

1. Asphyxiants: *e.g.*, carbon monoxide and cyanogen compounds.

2. Irritants: *e.g.*, sulphur dioxide, chlorine, sulphuretted hydrogen, nitrous fumes.

3. Volatile drugs and drug-like substances: *e.g.*, anæsthetics, tetrachlorethane, benzene, carbon bisulphide, nitrobenzene, carbon tetrachloride, trinitrotoluene.

**Carbon Monoxide.**—In the treatment of carbon monoxide poisoning the sheet anchor is the inhalation of oxygen containing 7 per cent. of carbon dioxide. The inhalation treatment by  $O_2$  and  $CO_2$  was introduced about 1921: originally the mixture recommended contained only 5 per cent.  $CO_2$ , but about 1929 the proportion was raised to 7 per cent. with excellent results.

The mixture of carbon dioxide and oxygen is available in cylinders of the compressed gases. It should be administered by one of the techniques described in the section on oxygen therapy, preferably through a B.L.B. mask (see p. 956).

Artificial respiration may be necessary. If so, the oxygen-carbon dioxide mixture should be administered while it is being carried out. The inhalation of oxygen and  $CO_2$  should be continued for at least twenty minutes after spontaneous respiration commences. It is important that the patient be kept warm by the use of blankets and hot-water bottles while inhalation treatment is being carried out.

Blood transfusion has been recommended, but it is useless unless performed within an hour of removal from the gas, which is seldom practicable under industrial conditions. Later the elimination of carbon monoxide renders transfusion unnecessary: the patient is by that time suffering from the late effects of asphyxia, which are not relieved by transfusion. German observers report that massive venesection is often of value in these cases.

Drugs are of little value in the treatment of asphyxia, though from time to time various respiratory stimulants have been advocated in this connection: in 1924 the German Imperial Health Office reported favourably on Lobeline Ingelheim as a respiratory stimulant (3 to 10 mg. intramuscularly). For some years the injection of methylene blue had a vogue, but it has now been discredited in the treatment of carbon monoxide poisoning.

Headache is apt to be persistent. It is due to increased intracranial pressure and is best treated by venesection or by the intravenous administration of hypertonic saline (70 to 100 c.c. of a 15 per cent. solution). Phenacetin, aspirin, etc., should not be given to relieve headache, as severe attacks of heart failure have followed the giving of these in gas poisoning.

It is essential that persons who have been gassed should have prolonged rest. The patient should not be allowed to walk home from work after recovery. After-treatment consists of general measures designed to prevent the development of pneumonia.

**Cyanogen Compounds.**—Hydrocyanic acid should be used with the utmost precaution. Of recent years it has had an extensive vogue in the disinfection of ships and premises, and accidents have occurred from failure to adhere to the necessary rigid instructions governing effective clearing of the atmosphere before re-entry.

Treatment of hydrocyanic acid poisoning is along lines similar to those described for carbon monoxide poisoning and consists essentially of artificial respiration and the inhalation of the oxygen-carbon dioxide mixture described above. Lobeline (10 mg. intravenously) has been found to be of service, and the consensus of opinion appears to be that methylene blue is of some value in the treatment of poisoning by hydrocyanic acid: the recommended dose is 50 c.c. of a 1 per cent. solution in physiological saline given intravenously.

After-care is the same as for carbon monoxide poisoning.

**Nitrous Fumes.**—When symptoms of poisoning from nitrous fumes occur while the patient is still at work, the appropriate first-aid treatment is to make him lie down, keep him warm and, in the presence of cyanosis, to administer oxygen. Much of the danger of these nitrous gases lies in the fact that there is often a lag of several hours between exposure to them and the appearance of acute symptoms, which often rapidly assume the alarming clinical picture of pulmonary oedema. Medicinal measures contribute little to the relief of this condition, though sometimes it is improved by the intravenous administration of saline solution, combined with venesection where cyanosis is marked. Bleeding, followed by the intravenous injection of glucose, is recommended by Professor Zangger. Inhalation of oxygen, preferably through a B.L.B. mask (see p. 956), is often of great value. It is important to secure absolute quiet and rest, otherwise cardiac failure is liable to supervene.

**Chlorine.**—Chlorine is a typical irritant gas and its inhalation is apt to produce generalized inflammation throughout the respiratory tract. There used

to be a tradition that the inhalation of low concentrations of chlorine is of value in the prevention of diseases of the respiratory tract, and over a hundred years ago Thackrah actually treated the bronchitis of flax-workers by the inhalation of chlorine, placing his patients for this purpose in a room artificially impregnated with the gas. This method of treatment is, of course, strongly contraindicated.

In first-aid treatment of chlorine poisoning it is important to keep the patient at rest, as exertion causes him to breathe more rapidly and deeply and thus inhale more of the irritant gas. The patient should be wrapped up warmly. Black coffee is a useful stimulant. Severe cases of chlorine poisoning demand the adequate administration of oxygen containing 7 per cent.  $\text{CO}_2$ . The main essential is to combat pulmonary oedema, and this can probably best be done by giving oxygen and by profuse blood letting (up to 1,200 c.c.). Blood transfusions are contraindicated. The administration of 15 minims (0.9 c.c.) of tincture of opium may be necessary to allay restlessness.

There has been considerable controversy as to the desirability of giving morphine for the relief of cough following the inhalation of chlorine; most authorities are agreed that it should not be used. Steam inhalations have been found serviceable in this connection.

**Sulphuretted Hydrogen.**—In the first-aid treatment of poisoning by this gas it is important to secure immediate removal of soiled clothes.

The treatment of acute poisoning by sulphuretted hydrogen consists in artificial respiration combined, where necessary, with the inhalation of oxygen containing 7 per cent. carbon dioxide. General symptomatic treatment and after-care are as for other poisonous gases.

For the irritation of mucous membranes which the gas is apt to produce when present in comparatively low dilutions, bland symptomatic treatment is all that is necessary. These local irritating effects tend to occur in epidemics which are best cut short by attention to workroom ventilation.

**Phosgene.**—Absolute rest is essential. First-aid treatment consists in the inhalation of oxygen containing 7 per cent.  $\text{CO}_2$  or, failing that, of pure oxygen. The patient must not be allowed to walk about and should go to hospital by ambulance. Serious pulmonary oedema may suddenly supervene after a few hours in patients who do not at first appear to be seriously affected. On this account the patient must be closely watched for twenty-four to forty-eight hours. Continuous administration of oxygen by means of a mask may be required for several days.

**Methyl Alcohol.**—Methyl alcohol has long been recognized as a poison causing either death or blindness in a large proportion of cases. During the war, American workers obtained good results from intensive alkali treatment. Intoxication by methyl alcohol upsets metabolism, giving rise to a profound acidosis, with excessive amounts of lactic and other organic acids excreted in the urine. The onset of symptoms is often delayed from 9 to 36 hours, when suddenly weakness, headache, nausea and epigastric distress appear, associated with dimness of vision. Along with general measures to combat shock, immediate steps should be instituted to eliminate the acidosis (see p. 783): the plasma carbon dioxide combining power may be reduced to 10 volumes per cent. It may be necessary to continue intensive treatment along these lines for four or five days. It is important to keep the eyes covered until all visual and retinal changes have disappeared.

**Carbon Tetrachloride.**—Carbon tetrachloride is widely used as a non-inflammable solvent for extracting grease (rapid cleaning processes) and as a fire-extinguishing fluid. Immediate mortality due to the acute narcotic effect of the fumes is of comparatively rare occurrence, but many cases have been recorded where death has followed at an interval of three to twelve days after severe exposure.

The treatment of acute poisoning by carbon tetrachloride is as described for carbon monoxide.

The treatment of subacute and chronic cases consists in removal from the causal work, plenty of fresh air and alkalization—with sodium carbonate, calcium carbonate or intravenous calcium gluconate; calcium therapy may well be combined with the administration of dextrose or glucose drinks. Graham has described a case of poisoning by carbon tetrachloride in which acute abdominal symptoms predominated and in which he obtained striking improvement from the intravenous injection of 10 c.c. of a 10 per cent. solution of calcium chloride.

Recently American workers have found methionine of value in the treatment of hepatitis in poisoning from carbon tetrachloride: doses of 2 gm. are given intravenously in saline every four hours—as much as 65 gm. in all may be given without untoward effect. This treatment may be combined with a high-protein, high-carbohydrate, low-fat diet.

In some patients the symptoms of renal injury overshadow those of damage to the liver. In these cases the early signs and symptoms—nausea, vomiting, jaundiced scleræ and tenderness of the liver region—are followed by the development of symptoms of uræmia, for the treatment of which see p. 783.

**Tetrachlorethane.**—Poisoning by tetrachlorethane was a major problem during the war of 1914-18, and a drastic code of preventive measures was adopted to deal with it. These measures included effective local ventilation by exhaust fans placed at floor level, and also involved fortnightly medical examination of the workers.

Blood examination is a useful check on a man's fitness for work. The hæmatology required, however, calls for special technical skill and is beyond the scope of general practitioner's work. The characteristic changes occur *before* clinical symptoms develop. Thus an individual who has been complaining for a few days of loss of appetite and sleeplessness would, in the face of abnormal blood findings, be laid off work for a week; while a man with the same symptoms but a normal blood appearance might be allowed to continue at work, though under close clinical and hæmatological supervision. With more severe symptoms or with any abdominal pain, a man should be suspended from work immediately; he will probably require two or three weeks off work. If symptoms reappear after a period of rest the man should be transferred to other work.

Willcox recommended in mild cases rest, a light diet rich in carbohydrates, but poor in fat and protein; in cases with marked jaundice the administration of glucose and of alkalis (sodium citrate and sodium carbonate, 2 gm. of each in solution four times a day), with in extreme cases venous, subcutaneous or rectal infusions of normal saline containing 8 gm. of sodium bicarbonate to the pint. Suppression of urine may call for hot-air baths.

Desoilles and Mélinos have recommended injections of liver extract in daily doses corresponding to 60 gm. or more of fresh liver.

**Benzene.**—The absorption of even small amounts of benzene causes an increased proportion of the total sulphates of the urine to appear as organic salts. Experience has shown that the periodic determination of the inorganic fraction is a useful adjunct to medical supervision of workers exposed to benzene. A progressive fall below the normal 80 per cent. points to the need for thorough clinical and hæmatological overhaul of all workers.

The treatment of acute benzene poisoning is similar to that described above for carbon monoxide.

The treatment of chronic benzene poisoning is unsatisfactory. It consists largely in removing the patient from exposure and in measures directed to improvement of the general health, and to safeguarding the patient from intercurrent infection which he is ill-equipped to meet. The deleterious effects of benzene may continue to operate for some months after termination of exposure. Repeated blood transfusions are of value; they, and saline injections, are often necessary to tide the patient over periods of emergency. Treatment of agranulocytosis may be necessary (see p. 513).

Recently, liver therapy and a vitamin-rich diet (especially in vitamin C) have been recommended to combat the severe anæmia. In this country liver treatment has proved disappointing, but it is the considered view of the United States Public Health Department that in chronic cases with leucopenia liver therapy with iron and vitamin C should be administered.

**Nitro Derivatives of Benzene (Dinitrobenzol, trinitrotoluol, etc.).**—The prevention of poisoning by these involves limitation of exposure to the toxic agent, as by mechanical ventilation, protective clothing and alternation of employment. Workers should be carefully chosen, and those who have suffered from jaundice should be excluded. No one under the age of eighteen should be employed, and no female under 105 lb. in weight: women appear to be more susceptible than men to TNT poisoning. The first five months of work with TNT call specially for close medical supervision of sickness absenteeism and for weekly medical examination. Loss of weight and a fall of 15 to 20 per cent. in the blood hæmoglobin is to be regarded as a danger signal and an indication for suspension.

First-aid treatment consists in rest, removal of working clothes, cleansing of the skin, oxygen inhalation and, if necessary, artificial respiration. Hot black coffee is of value in the treatment of the headache and drowsiness that are common early symptoms.

For mild cases treatment consists in removal from work, correction of constipation (*cascara sagrada*), and a suitable diet (milk, milk puddings, fruit and vegetables). In some cases of poisoning by nitrobenzene rapid improvement results from the intravenous injection of methylene blue. Patients with jaundice should be confined to bed and given a bland high carbohydrate fluid diet. The administration of insulin and glucose has been found helpful in the promotion of detoxication in some severe cases of TNT poisoning. The tendency to acidosis should be counteracted by administration of alkalis (sodium citrate and sodium carbonate, 2 gm. of each in solution four times a day). Severe cases may require saline injections (rectally and intravenously): in these cases blood transfusion is valuable.

In cases of acute poisoning death usually results from paralysis of the respiratory centre. Treatment consists in the inhalation of oxygen and 7 per cent.  $\text{CO}_2$  combined with artificial respiration where necessary. The patient should be kept warm and absolutely at rest. Nothing should be

administered by mouth until the patient is fully conscious. Hypodermic medication should be avoided except when some physical injury requires morphia to overcome pain after termination of anæsthesia.

In the manufacture of toxic war gases such as chloroacetophenone (tear gas), diaphenylchloroarsine, diphenylaminechloroarsine (Adamsite) and dichloroethylsulphide (mustard gas) careful precautions must be taken to protect workers from contact with the gas. The plant should be well equipped with ventilators and should be kept spotlessly clean. The air should be changed constantly. All chemical reactions should be effected in sealed containers and the products of these reactions should be conveyed through sealed pipes to further containers without any exposure to the air. Gas masks should be used in all operations involving gases dangerous to the respiratory track.

The treatment of acute gassing is along the general lines indicated above.

## INDUSTRIAL DUST DISEASES

The prevention of industrial dust diseases lies primarily in measures for efficient dust control. There are several ways in which this can be secured, and the choice of the method to be used must depend on such considerations as the nature of the dust in question, whether the process lends itself to enclosure or to wet working and so on: many industries of high dust exposure have adopted systems of artificial exhaust ventilation, and such systems are in some industries required by law. It occasionally happens that workmen are necessarily exposed to dust in processes that do not lend themselves to any of these measures of control; then reliance must be placed on the use of respirators. The Mark IV respirator (made by Siebe, Gorman & Co. Ltd., Jarvis Road, Tolworth, Surrey) is probably the best of these: it has a filtering efficiency of over 95 per cent. against a dust cloud containing a high percentage of particles of a potentially dangerous size.

Since the war of 1914-18 an interesting medical step has been taken in Britain towards the prevention of silicosis and asbestosis. In an effort to combat these diseases Medical Boards have been set up at different points in areas where these diseases are particularly prevalent: the headquarters of the Chief Medical Officer of the Board are at 37 Exchange Street, Sheffield. The examinations carried out by these special Boards fall into three groups, (1) Initial, (2) Periodic, and (3) Compensatory. All entrants to the scheduled industries must be examined within one month of commencing work and are prohibited from entering the industry if their physique falls short on the score of abnormality of the nose or throat, existing heart or lung disease or general under-development.

The periodic examinations cover workers employed in the specified industries (refractories, sandstone, pottery, asbestos), and their frequency varies with the risk of the several processes, examinations being carried out annually where the risk is greatest. The Board have power to exclude from the industries workers found to be suffering from tuberculosis, and power to recommend for compensation workers suffering from silicosis or asbestosis. In the case of younger men suffering from simple silicosis there is power to order them to leave the industry with the award of a small amount of compensation designed to tide over any financial loss involved in their change of occupation, the idea being that these men should seek

more suitable work while yet their health is reasonably good. Older workmen found to be suffering from silicosis are advised to leave the industry and are offered compensation to enable them to do so.

It is open to any workman in the industries concerned to apply for medical examination by the Board with a view to obtaining compensation for pneumoconiosis, and it is open to the dependants of any deceased workman to make a similar claim, but this latter may involve post-mortem examination, and where such claims are contemplated it is advisable to communicate with the Chief Medical Officer of the Board before burial.

In 1941 a new scheme was introduced for the compensation of workers in certain processes in the cotton industry. This scheme makes provision for supplementing the National Health Insurance benefit of men who are totally disabled from byssinosis (a condition characterized by bronchitis and emphysema, but without diagnostic X-ray changes) provided they have been for more than twenty years in the employment. The Workmen's Compensation Act (1943) makes possible the compensation of workmen suffering from any form of pneumoconiosis (defined as including fibrosis of the lungs due to silica, asbestos or other dust, as well as "the condition of the lungs known as dust reticulation") and authorizes payment of benefit (as in byssinosis) to men employed in coalmining who are totally disabled but not otherwise entitled to compensation. Applications for allowances under the benefit scheme should be addressed to: The Secretary, Newport Road, Cardiff.

Silicosis and asbestosis tend to be progressive diseases, but their downhill course is accentuated by continued exposure to the causal dusts and by superadded infection. It follows that the aim should be to secure the withdrawal of affected workmen from exposure as early in the disease as possible. They should, so far as practicable, be protected from the rigours of strenuous work in unfavourable weather conditions. Many elderly stone-workers have found it serviceable to wear a layer of gamgee tissue on the chest. Otherwise the treatment is entirely symptomatic, though it is an extraordinary feature of silicosis that symptoms are often inconspicuous or absent even in the presence of advanced disease.

Experimental work in Canada and America suggests that the inhalation of finely powdered aluminium dust is of value in the prevention of silicosis in experimental animals, but further work is necessary to determine the value of the method to human beings under industrial conditions; inhalation of aluminium dust cannot be accepted as a substitute for adequate dust control. The therapeutic use of aluminium inhalation is claimed to relieve subjective distress in some cases, but caution is necessary in its use.

## INDUSTRIAL DERMATITIS

The potential causes of dermatitis encountered in industry are legion. Among the chief are alkalis, oil, friction and heat, chemicals, degreasing agents and sugar, and the workers most affected are engineers, chemical workers, dyers and calico printers, painters and paint manufacturers, metal workers, metal platers and polishers and textile workers. But the number of occupations at risk and the risks involved are so many that only the most careful clinical examination, together with a consideration of individual and occupational history, can serve to decide whether there is an occupa-

tional element; and the clinical examination should be supplemented by such investigations as patch tests wherever these are available.

In the recognition of skin sensitiveness to trade irritants, *e.g.*, nickel, tests may be applied by patch or drop methods. In the case of nickel, for instance, 8, 4 and 1 per cent. alcoholic solutions of chemically pure nickel chloride are used, a drop of each being placed on the skin, usually that of the abdomen; the alcohol quickly evaporates and in sensitive cases a local reaction occurs in from six to eight hours.

In the prevention of industrial dermatitis certain general procedures are helpful.

In the examination of new workers it should be borne in mind that some are more susceptible to dermatitis than others and that one attack often predisposes to another. Experience has shown that workers with a good healthy skin, preferably not too dry, are least likely to develop dermatitis.

Systematic and frequent inspection of the hands and arms of workers, if carried out by a responsible person, can be of value in detecting early signs of dermatitis—redness, cracks, blisters, etc. Early treatment should be obtained for any commencing irritation, and if the condition does not immediately respond the causal work should be stopped or changed until the skin condition clears up. Care and cleanliness on the part of the worker can do much to prevent dermatitis and should be encouraged by the provision of adequate washing facilities. If alkalis or other similar agents are used to remove stains from the hands, they should be used as sparingly as possible— $\frac{1}{2}$  lb. of bicarbonate of soda to 2 gals. of water makes a suitable alkaline solution: for this purpose a weak solution of sodium hyposulphite is also useful. Where chloride of lime is used for the removal of dyes from the skin of the hands it frequently causes irritation; this may be avoided by dipping the hands in a 10 per cent. solution of bisulphite of soda after using the chloride, then rinsing them in water. Such substances as methylated spirits and turpentine, which are sometimes used to remove stains, are themselves liable to produce dermatitis if used too frequently and allowed to remain on the skin too long. Vegetable oils should be substituted for these wherever possible. After the use of any cleansing agent it should be the invariable practice to wash with soap and water, then to rinse the hands and arms thoroughly in running water. The application of cold cream to the skin after washing is of value in preventing irritation.

Gloves worn for the prevention of dermatitis should be used with care. It is important that they should be free from holes and sufficiently tight fitting at the wrist to prevent irritants from getting into them. Prosser White points out that the use of waterproof gloves encourages heavy sweating, especially when working in hot liquids; perspiration soddens and removes the horny layer and this renders the skin tender, thin and vulnerable to any active chemical. The wearing of leather gloves seems to render the skin peculiarly susceptible to such infections as ringworm: in these cases benefit results from the local application of a powder containing salicylic acid (5 gm.), menthol (2 gm.), camphor (8 gm.), boric acid (50 gm.) and starch (35 gm.). Before gloves are used they should be scrupulously dry and clean inside and the hands should be dusted with talc or other suitable dusting powder.

Early and careful treatment of all injuries, however trivial, is of importance, as dermatitis frequently originates round an untreated sore.



Much experimental work has been done under the auspices of the Ministry of Labour towards the production of a satisfactory barrier substance that will be of value in the prevention of dermatitis. Barrier substances are designed to protect the skin against irritants. Different preparations are required for different types of work; it is not possible to produce one cream that will protect against all irritants. Certain criteria are applied to these barrier substances: they must be non-irritating to the skin; insoluble in the substances against which skin protection is specifically required; easily applied to the skin and reasonably stable on it, not becoming so dry as to cause the protective film to crack; non-slipping, so as not to interfere with manipulative dexterity; and easily removed after work without the aid of special cleansers. Paraprol, of which the essential constituents are urea, sodium alkyl sulphonate, benzyl alcohol and tragacanth, has been found of value in the prevention of industrial dermatitis in engineering factories using cutting oils. Lanolin has been found to be of service as a protective against mineral oil or tar dermatitis, and Henry has found pure liquid paraffin to be useful in the prevention of celery itch, a dermatitis occurring in the canning of celery.

The skin of the men exposed to the dust of lime after it has been burned becomes dry and may fissure, with the formation of painful ulcers. Protection against these sores has been obtained from talc powder shaken over the skin from a pepper pot. It keeps the skin dry and forms a protective film on the skin: strips of lint worn under the collar save the skin of the neck from being abraded.

Burns occurring on the exposed skin of cement workers are usually secondarily infected and are not readily cured by tannic acid, gentian violet or silver nitrate. The crust should be loosened with olive oil, and when the underlying simple acute ulcer has been cleared up and granulations appear, cod-liver oil ointment often hastens healing. Pitch dermatitis can be controlled by thorough personal hygiene. Among outdoor workers the incidence can be reduced by the avoidance of work in bright light, rotation of work and selection of tolerant personnel.

Warts in fish workers clear up rapidly when the "parent" wart is removed by one of the usual methods of treatment, such as by the application of strong acids or the electric needle.

In the prevention of dermatitis from machine lubricants, it has been found of service to protect the oil from dust, to strain it free from extraneous material and to renew when it becomes contaminated; Bridge advises filtering and heating to a temperature of 300° F.

The prevention of chrome ulceration and dermatitis is facilitated by the care of cuts and abrasions and the protection of the hands with a suitable ointment (lanolin). Dressings should be protected from water by impermeable coverings. Skin ulcers can be treated by the application of boracic fomentations and the subsequent use of an ointment containing ichthyol gr. v to the ounce. Exposure to ultra-violet light has proved useful. For chrome ulceration of the nasal mucous membrane it is generally sufficient to apply a little liquid paraffin on plugs of cotton-wool.

For treatment of established cases of dermatitis the steps to be taken are: (a) removal from contact with the offending irritant; (b) attention to the general health (which is important); and (c) local treatment, the removal of crusts by the application of a boracic starch poultice and the application

of an ointment containing 5 gr. (0.3 gm.) to the ounce of ammoniated mercury in zinc paste. Where large areas are affected boro-calamine lotion may be used with advantage. In old-standing chronic cases the application of crude gas tar is worthy of trial.

Special agents have been found to be of service in dealing with dermatitis from particular sources. Thus Prosser White favours the treatment of all dermatoses caused by plants by the immediate application of watery solutions of alkalis. In the treatment of "tulip fingers" the use of biniodide spirit, along with the wearing of gloves, has been found to be effectual, while in the treatment of "grain itch" (due to *pediculoides ventricosus*) mere application of soap and water is sufficient treatment.

Dermatitis is the commonest affection due to work in the manufacture of the commoner poisonous gases used in war and mentioned on p. 335. It is usually due to carelessness of the worker in the use of protective clothing—temporary removal of gloves, badly fitting gloves, etc., though it must be remembered that rubber and leather do not protect from mustard gas. The hands and face should be carefully washed before partaking of food—in a separate room from the workroom. Even before leaving the factory the worker should bathe and change to street clothes; there should be a change of work clothes every two days.

Tetryl, used in the manufacture of high explosives and belonging chemically to the TNT group, often produces severe dermatitis affecting hands, face and neck. Males are especially vulnerable, and individuals vary greatly in susceptibility. Hair protection is difficult, but important; varnishes are useful protective skin applications.

It is found that with all products other than mustard gas it is helpful to wear rubber gloves and a cotton suit impregnated with linseed oil. It is important to secure immediate treatment of areas affected, or suspected of being affected by diphenylchloroarsine, with a fresh solution of sodium hypochlorite (0.5 per cent.) for one hour. Where burns or dermatitis occur after contact with these gases chloramine cream or a 1 to 4 per cent. aqueous solution of chloramine-T should be used, on the theory that chlorine unites with the toxic gas to form a non-toxic product. Where large bullous lesions occur the top of the blister should be removed with sterile scissors and forceps and a 5 per cent. solution of methylrosaniline in 20 per cent. alcohol applied. The patient should be given frequent baths of potassium permanganate (1:3,000 or 1:4,000). This astringent, emollient and mildly antiseptic treatment prevents infection, keeps the parts dry and promotes rapid healing. Areas affected by chloroacetophenone (tear gas) should be treated immediately with a 20 per cent. solution of sodium bicarbonate and hot local applications.

For general treatment of dermatitis (eczema), see p. 179.

## INDUSTRIAL CANCER

The measures for the prevention of industrial cancer may be regarded as falling into two broad groups: (a) those aiming at limitation of contact with carcinogenic substances; and (b) those involving medical supervision of the health of the worker. The first group includes such procedures as the substitution for carcinogenic oils of others not possessing those properties, and it has been demonstrated that there is considerable scope for substitu-

tion of this kind; alternation of employment; the provision of baths and of suitable changing facilities at the works; and the protection of the skin by suitable local application. Where the irritant is dusty, it has been found serviceable to dust exposed parts with zinc oxide and starch before commencing work. Where it is oily, as in work with paraffin, Scott has recommended smearing of the skin with either commercial castor oil or an ointment containing equal parts of olive oil and lanolin. A large jar of the protective substance is kept available or supplies issued to the men at weekly intervals, and they are encouraged to use it freely, *e.g.*, whenever they dry their arms after washing.

Thorough medical inspection of the skin of workers should be carried out at regular intervals (monthly to quarterly, depending on risk involved). It is important that accurate records should be kept of conditions found at each examination, so that deterioration can be promptly detected. New workers should be carefully observed, and those found to be particularly susceptible to papular dermatitis shortly after commencing work should be discouraged from continuing in the industry.

Successful treatment aims at the anticipation of malignant degeneration. Removal of warts by carbon dioxide snow and free excision, or other appropriate treatment (radium), of suspicious or malignant ulcers is indicated; the results, if treatment is undertaken sufficiently early, are good. It has long been observed that the application of radium has a highly beneficial effect on warty conditions due to exposure to X-rays.

Brodie has reported good results from the electro coagulation of ulcers undergoing malignant degeneration.

To safeguard the health of workers exposed to the risk of bladder tumours (from contact with aniline and allied dyestuffs), clinical supervision of the workmen, reinforced by routine microscopic examinations of urine, are of value. If red blood cells are found in the urine, the worker should be examined cystoscopically. The further treatment is essentially surgical and should be instituted as early as possible.

## **INJURY FROM RADIO-ACTIVE SUBSTANCES AND ULTRA-VIOLET RAYS**

Of recent years much thought has been given to the protection of workers exposed to radio-active substances. The British X-ray and Radium Protection Committee (Dr. A. E. Barclay, Chairman) first issued recommendations on the subject in 1921, and issued its sixth revised report in 1946. The dangers of over-exposure to X-rays and radium can be avoided by the provision of adequate protection and suitable working conditions. Such protection is necessary to guard against injuries to the superficial tissues, changes in the blood and damage to other internal tissues, particularly the generative organs. It is recommended that for whole-time radium and X-ray workers hours of work should not exceed seven per day and five days per week, the off-days to be spent as much as possible out of doors; that there should be not less than four weeks holiday per year, preferably consecutively; that no person should be employed on this work whose blood condition (on complete investigation) or general health is unsatisfactory; and that the amount of X or  $\gamma$  radiation received by oper-

ators should be systematically checked to ensure that the tolerance dose is not exceeded, photographic films or small capacity condensers being carried on the person for that purpose. As an additional precaution, workers may be tested for the amount of radium in their bodies by direct gamma-ray measurement or by measurement of the concentration of radon in their expired breath. The National Physical Laboratory has established a service to test the amount of radiation received by X-ray or radium workers: this is carried out by means of sensitive photographic films which, after exposure to working conditions, are developed under rigid control.

Before the commencement of exposure to radio-active substances, the normal leucocyte level should be determined by making three total and differential blood counts in the afternoon. If none of the total counts reach 6,000 per c.mm. and none of the lymphocyte counts reach 1,200 per c.mm., the applicant should not be accepted for service. Periodical total and differential blood counts of the worker should be made during the afternoon once every six months in the case of X-ray workers and once every three months in the case of radium workers. If at any time there is found to be a decided and sustained drop in either the total leucocyte or the total lymphocyte count the worker should cease work and be placed under treatment for an adequate period. On resumption of work the health should be carefully supervised and working conditions thoroughly scrutinized to prevent a recurrence.

The British Report cited above contains precise directions on such matters as construction of workrooms, working temperatures, etc., and technical information about the nature of adequate protection from the action of radio-active substances.

Though these recommendations are framed primarily to safeguard the health of scientific workers, they apply with equal force to the industrial use of radio-active substances, *e.g.*, people working with luminous paints. Indeed, where X-ray screening is carried out continuously over long periods the protection afforded requires to be even greater than that specified for hospital practice. In any case, the protective arrangements and working hours should be such that the radiation received by the operator does not exceed 1r per week.

The Minister of Labour has recently issued a new code of rules for the protection of those working with radio-active substances [The Factories (Luminizing) Special Regulations, 1947] in which it is laid down that in addition to the protective measures hitherto in use and described above all employees working with or near luminous compound shall be examined within seven days of starting work, and thereafter at intervals of not more than one month, and a Health Register, to include all employees, must be kept. There are also limitations of employment to the effect that not more than forty-eight hours must be worked in a week and that three months must be spent in other employment after each full year's employment on processing.

It is well known that open and closed arcs yielding ultra-violet radiation are dangerous to the naked eye. During their use goggles of proved opacity to ultra-violet rays should be worn by patients and by operators. Their opacity can only be proved satisfactorily by a spectroscopic test, and goggles which transmit radiation shorter than 3,800 A.v. should not be used. Prolonged exposure to ultra-violet radiation produces pigmentation

of the skin, which may be prevented by wearing thin muslin over the face.

The ventilation of rooms used for ultra-violet therapy is of importance, since all arcs produce deleterious gases and open arcs also consume oxygen. It is generally necessary to secure artificial ventilation by exhaust fans.

The only effective treatment for the systemic disturbance of workers suffering from over-exposure to radio-active substances lies in immediate removal from the working environment, attention to the general health under good open-air conditions and a prolonged holiday before return to work, with the subsequent preventive care noted above.

The treatment of injury to the superficial tissues depends on the nature and severity of the lesion. It should never be regarded lightly and may well call for consultation between dermatologist, radiotherapist, physician and surgeon.

T. FERGUSON.

# METABOLIC DISEASES

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## DIABETES MELLITUS

### DIETETIC TREATMENT

**T**HERE are, perhaps, few diseases which the average doctor feels himself less qualified to treat than diabetes mellitus. Yet the wise management of a previously untreated case can almost be guaranteed to give the patient dramatic relief from his symptoms, and to produce a striking improvement in his general health, a therapeutic claim which can, unfortunately, be made with confidence in only a few other medical conditions. The reason for this disinclination to treat diabetes probably lies in the common belief that in order to do so efficiently a profound knowledge of dietetics is necessary, with an ability to calculate diets in terms of their total calories, their glucose : fatty acid ratio, and their fat, protein and carbohydrate content. Most doctors know perfectly well that even if they could calculate diets in this way, it would take them a considerable part of their working day to do one such diet accurately. In consequence, some resign themselves to the belief that the treatment of diabetes is the province of specialists or content themselves by advising their patients in a general way to cut down their intake of sugars and starchy foods.

Apart from the exceptional case, and apart from diabetes in children, this exaggerated belief in the difficulty of treating the condition is unfounded. Successful treatment demands the possession of a good dietetic system with a knowledge of how to use it and how to adapt it to the requirements of the patient. The doctor need not work out the actual details of the diet himself. He does not, after all, gather his own herbs and prepare from them his own medicines. Rather he prescribes doses of certain drugs and his prescription is made up into the medicine by a pharmaceutical chemist. Similarly, he should be able to prescribe the dose of calories and carbohydrate suitable for his diabetic patient, and his prescription can be worked out for him by a dietitian.

A dietitian, however, is not always available, and in the following pages an attempt has been made to describe a simple dietetic system for the treatment of the average diabetic, which in all but exceptional cases should make the introduction of the dietitian or specialist superfluous. By the use of exchange lists a great number of foodstuffs can be utilized, provided they are used in their proper proportions, so that there is no need to limit the diabetic to a dull and monotonous menu, and no need for him to use patent diabetic foods, which are often expensive and usually unappetizing.

Recently there has been a strong tendency to deride the careful dietetic treatment of diabetes. It has been held that hyperglycæmia in itself is harmless provided a sufficient metabolism of carbohydrate is maintained to prevent ketosis and to avoid undue loss of weight. The protagonists of this hypothesis suggest that patients should be allowed to eat what they like and what their appetites dictate, insulin being used in doses calculated

only to avoid ketosis, polyuria and undue loss of weight on the one hand and hypoglycæmia on the other, little or no notice being taken of hyperglycæmia or glycosuria. It will be appreciated how enthusiastically this advice will be received by patients anxious to avoid the irksome restrictions of diabetic dieting and by practitioners unwilling to master its relatively simple principles. We agree that in the past diabetic dieting may often have been over-meticulous and restrictive and that the ideal of a completely sugar-free urine for severe diabetics, and especially for diabetics with a low renal threshold for sugar, may be undesirable, and if attempted may result in unpleasant hypoglycæmic reactions. Nevertheless we should be very chary of discarding dietetic treatment which has stood the test of time without a great deal more proof that the health of those diabetics, who are allowed to be continuously hyperglycæmic with a heavy glycosuria, does not suffer in the long run, that their sugar tolerance does not steadily deteriorate so that they require larger and larger doses of insulin and that they are not rendered unusually prone to the development of infections.

**The Calorific Value of the Diet.**—Many people in this country eat more food than is necessary for them to maintain their weight and to give them energy for their various activities. This does not mean that many people are not undernourished; but they are undernourished from eating diets deficient in certain foods, rather than from eating too little food as a whole. Many of us, then, eat more calories than we actually require. In a few unfortunate individuals these excess calories are promptly stored in the form of fat, but in the great majority they are successfully burnt up and dissipated in the form of heat.

The diabetic individual has difficulty to a greater or less extent in metabolizing food, especially carbohydrate food. The first principle, therefore, of diabetic dieting consists in cutting out the excess food consumption in which many indulge. In other words, we should give the diabetic sufficient calories, and no more, to give him energy for his particular activities and to maintain him at his ideal weight, or slightly below it, for no diabetic should be allowed to become much overweight.

It is apparent that the number of calories required will vary considerably according to the age, sex, weight, height and particular activities of the diabetic concerned. For example, an elderly, small fat female of sedentary habit will require considerably fewer calories than a young, tall, underweight, hardworking male. The first will probably benefit by being given a 1,000 or 1,200 calorie diet to bring her down to near her ideal weight, and will thereafter require not more than about 1,600 or 1,800 calories to maintain her at that weight and to satisfy her moderate energy requirements. The second, on the other hand, may need as much as 2,800 or even 3,000 calories to bring him up to near his ideal weight (though such high diets should only be given in exceptional circumstances), and he may thereafter require some 2,600 calories to maintain him at that new level and to give him energy for his strenuous life. In between these two extremes lie the majority of diabetics, who will thus require diets varying in caloric value between 1,800 and 2,600, according to the particular circumstances of the case.

**The Carbohydrate Content of the Diet.**—Since carbohydrate is the food which diabetics have most difficulty in metabolizing, it would at first hand appear reasonable to reduce the carbohydrate content of the diet to the

lowest possible limits. This was indeed the aim of dietetic treatment in the pre-insulin days and for a good many years after its discovery. A limit to carbohydrate reduction was set by the danger of inducing ketosis. It is well known that fats are inadequately metabolized and ketones make their appearance in the circulation if the carbohydrate content of a diet is reduced below a certain minimum, or if the proportion of available glucose to fatty acid in the diet is reduced below the ratio of 1 to 1.5. The ratio between available glucose in the diet and its fatty acid content—the G : FA ratio—thus became a matter of importance, and for many years the aim of treatment in diabetes was to give a diet in which there was only just sufficient available glucose, but no more, to ensure proper combustion of the fats. We were then rather like yachtsmen attempting to sail just as close as possible to the wind without losing it altogether. Diets calculated in this way rarely contained as much as 100 gm. of carbohydrate and their high proportion of fat made them unappetizing and somewhat nauseating.

Nowadays we realize that it is undesirable for the carbohydrate in diabetic diets to be so rigorously restricted. Patients feel better on a more liberal allowance and the diets so constructed are much pleasanter to take. Further, modern research has shown that diabetics on a very low carbohydrate intake are less sensitive to insulin than they are when a more adequate allowance is made. Thus, if a diabetic is taking insulin the dosage is not necessarily higher on a carbohydrate intake of rather over 100 gm. than it is on one of under 100 gm. This also applies to endogenous insulin secretion. In the healthy subject, for example, it is well known that the form and duration of the blood-sugar curve is conditioned by the constitution of the diet which the individual has been taking previously; after a period on a low carbohydrate diet, ingestion of glucose leads to a much higher and more prolonged rise in the blood sugar than is the case when the subject has been taking a high carbohydrate diet. This suggests that carbohydrate is a stimulus to insulin formation, and if it is too rigorously controlled in the diabetic a further inhibition of an already poor supply may occur. The rationale of the high carbohydrate diet is based on this phenomenon.

We believe that the average diabetic in this country requires for maintenance 130 to 200 gm. of carbohydrate a day, depending on his caloric requirement. Where this is low, 130 to 145 gm. of carbohydrate is usually sufficient; where relatively higher calories are needed, 160 to 200 gm. of carbohydrate should be given.

When a patient with *mild* diabetes first comes for treatment it is usually wise to attempt to get him "sugar-free" by dietetic means alone without the use of insulin. With this object in view we usually prescribe temporarily a low diet with a carbohydrate intake of 100 gm. and a caloric value of about 1,500 (see Diet Sheet I). Should he become "sugar-free" on this diet his calories and carbohydrate are gradually built up to his required maintenance level, and insulin is only administered should he stick half-way up the dietetic ladder. If, after a week or so on the initial low diet, he still has glycosuria, no further attempt is made to get him "sugar-free" by further dietetic restriction, since if he is unable to tolerate such a diet he will invariably require insulin either temporarily or permanently. He is, therefore, given without more ado the calories and carbohydrate which it is thought he will need to maintain his weight and to give him sufficient energy



to satisfy his requirements, and insulin is started in gradually increasing doses till he is "sugar-free." It is then often found that the patient has reacquired a good deal of his sugar tolerance, and the dose of insulin can sometimes be reduced and occasionally dispensed with altogether. It is a common fallacy to suppose that insulin once started will invariably be required permanently.

When, on the other hand, the diabetic, on his first visit, is found to be significantly underweight and to have definite acetone as well as sugar in the urine, no attempt should be made to get him "sugar-free" without insulin on the reduced calorie and carbohydrate intake mentioned above. The danger of producing an increased ketosis, and possibly coma, by such measures is a very real one, and insulin should be started at once with a diet containing 130 to 160 gm. of carbohydrate and a moderate fat content of 90 to 130 gm. When the sugar and acetone in the urine are controlled, the diet may be increased to meet the individual requirements.

#### DIET SHEET I

Cho. 100 gm. P. 68 gm. F. 88 gm. Cals. 1,464

(Unsuitable for prolonged use)

##### *Breakfast—*

Bacon,  $1\frac{1}{2}$  oz. or exchange (see p. 351).

Bread,  $1\frac{1}{2}$  oz.

Tea or coffee.

Butter and milk from allowance.

##### *Dinner—*

Clear soup, bovril or marmite, if desired.

Cooked lean meat, 2 oz.

Vegetable from Group I, large helping, or vegetable from Group II, one tablespoonful (see p. 350).

Orange,  $3\frac{1}{2}$  oz. or exchange (see p. 351).

Milk from allowance for curds or coffee, etc.

##### *Tea—*

Cheese,  $\frac{3}{4}$  oz. or 1 egg or exchange (see p. 351).

Salad of vegetable from Group I, if desired.

Bread,  $1\frac{1}{2}$  oz.

Tea.

Butter and milk from allowance.

##### *Supper—*

Cooked lean meat, 2 oz. or exchange (see p. 352).

Vegetable as at dinner.

Bread,  $1\frac{1}{2}$  oz.

Tea or coffee.

Butter and milk from allowance.

*Daily—*Butter or margarine, 1 oz. ; Milk, half-pint.

All food should be weighed after cooking except bacon, which is weighed before cooking.

**The Fat and Protein Content of the Diet.**—Of late years there has been a tendency in many schools to break away from the extremely meticulous dietetic directions of the past as regards protein and fat and to adopt a *laissez faire* attitude in regard to these constituents of the diabetic's diet. The rule of several dietetic systems has been "take care of the carbohydrate and the protein and fat will take care of themselves." We believe this attitude to be a wrong one. In order to obtain the best results, carbohydrate, protein and fat should all be accurately prescribed at the beginning of treatment. The patient should be carefully instructed in the weighing of food and in all the simple food exchanges. After two or three months of this regimen he becomes so familiar with quantities and exchanges that he is able gradually to dispense with the use of scales and to estimate the required amount of food with remarkable accuracy. What was in the first few weeks a most tedious and time-consuming exercise becomes eventually a simple matter of habit which need not handicap the individual concerned to any significant extent.

**The Calculation and Prescription of the Diet.**—From what has been said it will be apparent that if it is decided that a patient requires a diet of between 2,200 and 2,300 calories containing 160 gm. of carbohydrate, and a protein ration of, say, 98 gm., the remaining calories will be obtained at the expense of fat, and this quantity can easily be calculated. For clinical purposes the calories obtained from carbohydrate and protein can be calculated by multiplying the number of grams of each in the diet by four. In the example given this will equal 1,032 calories. On subtracting this figure from the total calories (*i.e.*, 2,265), 1,233 calories are left to be supplied by fat. Since each gram of fat gives on combustion 9 calories, the number of grams of fat required will be  $\frac{1233}{9}=137$ . Thus the diet will be prescribed as 160 gm.

of carbohydrate, 98 gm. of protein, 137 gm. of fat and total calories 2,265.

Three maintenance diabetic diets (Diet Sheets II, III, IV) have been set out in detail, and suggestions for increasing or decreasing the food value of these are given below. By use of the simple exchanges given on pp. 350-352, a varied diet can be taken by the patient each day.

The most convenient way of increasing the carbohydrate content of a diet is by the addition of bread. One ounce (30 gm.) of bread gives 15 gm. C. and 3 gm. P. It is therefore a simple matter to add or deduct the necessary amount of bread to give the desired carbohydrate. Not every patient desires his additional carbohydrate in the form of extra bread and, when required, one of the several alternatives for bread given on p. 352 may be used.

When the quantity of bread is altered the allowance of butter should also be adjusted. Approximately one-quarter the amount of butter to bread is a reasonable allowance. That is, if 2 oz. bread have been added, then add also  $\frac{1}{2}$  oz. butter. The addition of 1 oz. bread plus  $\frac{1}{4}$  oz. butter will increase the diet by 15 gm. C. and 135 Cals.

Thus, if an intermediate stage between Diet II and Diet III is desired, the above addition could be made to Diet II. If, on the other hand, the aim is to increase the calories but to allow the carbohydrate to remain constant, one of the following alterations could be made.

*Suggestions for increasing Calories without altering Carbohydrate Value*

The addition of butter 1 oz. gives 230 calories.

„	meat 1 oz.	„	75	„
„	one egg	„	78	„
„	bacon 1½ oz.	„	230	„
„	cheese 1 oz.	„	112	„

## DIET SHEET II

Cho. 130 gm. P. 80 gm. F. 107 gm. Cals. 1,800

*Breakfast—*

Bacon, 1½ oz. or exchange (see p. 351).

Bread, 1½ oz.

Tea or coffee.

Butter and milk from allowance.

*Dinner—*

Clear soup, bovril or marmite, if desired.

Cooked lean meat, 2 oz. or exchange (see p. 352).

Potato, 2½ oz.

Vegetable from Group I, large helping, or vegetable from Group II, one tablespoonful (see p. 350).

Orange, 3½ oz. or exchange (see p. 351).

Milk from allowance for curds or coffee, etc.

*Tea—*

Cheese, ¾ oz. or 1 egg or exchange (see p. 351).

Salad of vegetable from Group I, if desired.

Bread, 1½ oz.

Tea.

Butter and milk from allowance.

*Supper—*

Cooked lean meat, 2 oz. or exchange (see p. 352).

Vegetable as at dinner.

Bread, 1½ oz.

Tea or coffee.

Butter and milk from allowance.

*Daily*.—Butter or margarine, 1½ oz.; Milk, 1 pint.

## DIET SHEET III

Cho. 160 gm. P. 98 gm. F. 137 gm. Cals. 2,265

*Breakfast—*

Bacon, 1½ oz. or exchange (see p. 351).

Bread, 2 oz.

Tea or coffee.

Butter and milk from allowance.

*Dinner—*

Clear soup, bovril or marmite, if desired.

Cooked lean meat, 3 oz.

Potato, 3 oz.

Vegetable from Group I, large helping, or vegetable from Group II, one tablespoonful (see p. 350).

Orange, 3½ oz. or exchange (see p. 351).

Milk from allowance for curds or coffee, etc.

*Tea—*

Cheese, 1½ oz. or exchange (see exchange for egg, p. 351).

Salad of vegetable from Group I, if desired.

Bread, 2 oz.

Tea.

Butter and milk from allowance.

*Supper—*

Cooked lean meat, 2 oz. or exchange.

Vegetable as at dinner.

Bread, 2¼ oz.

Tea or coffee.

Butter and milk from allowance.

*Daily*—Butter or margarine, 2 oz. ; Milk, 1 pint.

## DIET SHEET IV

Cho. 200 gm. P. 110 gm. F. 158 gm. Cals. 2,660

*Breakfast—*

Bacon, 1½ oz. or exchange (see p. 351).

Egg, 1 or exchange (see p. 351).

Bread, 3 oz.

Tea or coffee.

Butter and milk from allowance.

*Dinner—*

Clear soup, bovril or marmite, if desired.

Cooked lean meat, 3 oz. or exchange (see p. 352).

Potato, 3 oz.

Vegetable from Group I, large helping, or vegetable from Group II, one tablespoonful (see p. 350).

Orange, 3½ oz. or exchange (see p. 351).

Milk from allowance for curds or coffee, etc.

*Tea—*

Cheese, 1½ oz. or exchange (see exchange for egg, p. 351).

Salad of vegetable from Group I, if desired.

Bread, 3 oz.

Tea.

Butter and milk from allowance.

*Supper—*

Cooked lean meat, 2 oz. or exchange (see p. 352).

Vegetable as at dinner.

Bread, 3 oz.

Tea or coffee.

Butter and milk from allowance.

*Daily*—Butter or margarine, 2½ oz. ; Milk, 1 pint.

It is, of course, of the utmost importance to study the character of the patient concerned. There are many who require to be warned continually of the necessity of dietetic care, and may indeed occasionally have to be frightened into being more accurate by a lecture on the considerable risk which they run by non-observance of the rules. Such treatment in other patients would turn them into hypochondriacs. Some over-anxious diabetics require the disease and its dangers to be minimized rather than stressed. Such patients should be encouraged to regard diabetes as an inconvenient idiosyncrasy rather than as a dreadful and ever-present menace, and that the occasional occurrence of a positive reaction in their Fehling test must not be regarded as a disaster of the first magnitude.

## VEGETABLES

(When fresh vegetables are unobtainable tinned ones may be substituted)

*Group I—*

1 to 3 per cent. Carbohydrate :

Mushrooms (no food value).	Cauliflower.	Cucumber.
Mustard and cress.	Artichokes.	Vegetable marrow.
Watercress.	Seakale.	Tomatoes.
Lettuce.	French beans.	Brussels sprouts.
Curly greens.	Eggplant.	Endive.
Celery.	Salsify.	Leeks.
Spinach.	Asparagus.	Rhubarb cooked with a pinch
Cabbage.	Radishes.	of baking soda.

*Group II—*

3 to 6 per cent. Carbohydrate :

Turnips.	Onions.	Carrots.
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*Group III—*

10 per cent. Carbohydrate :

Beetroot.	Parsnip.
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15 per cent. Carbohydrate :

Peas, fresh or tinned.

20 per cent. Carbohydrate (do not take without permission):

Potato.	Cooked dried peas, beans, lentils.
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### FRUITS (No tinned fruits)

$4\frac{1}{2}$ Oz.	$3\frac{1}{2}$ Oz.	=	$2\frac{1}{4}$ Oz.	=	$1\frac{1}{2}$ Oz.
$7\frac{1}{2}$ Per Cent.	10 Per Cent.		15 Per Cent.		20 Per Cent.
<i>Fruit.</i>	<i>Fruit.</i>		<i>Fruit.</i>		<i>Fruit.</i>
Grapefruit.	Gooseberries.		Apple.		Figs, dried.
Strawberries.	Orange.		Pear.		Prunes, dried
Blackberries.	Peach.		Apricots, dried.		Bananas.
Red currants.	Pineapple.		Plums, Victoria		
Black currants.	Greengage+stone.		+stone.		
White currants.	Cherries+stone.		Grapes.		
Cranberries.	Damson+stone.		Nectarine+stone.		
Raspberries.	Tangerines.				
Loganberries.	Apricots (fresh).				

### EXCHANGES FOR $1\frac{1}{2}$ OZ. BACON (RAW WEIGHT)

Calories—225

	Gm.	Approx. oz.	Remarks
Black sausage .	90	3	Omit $\frac{3}{4}$ oz. bread.
Cod roe .	120	4	Fried. Add $\frac{3}{4}$ oz. marg.
Cold boiled ham .	60	2	
Finnan haddock .	150	5	Add $\frac{1}{3}$ oz. margarine.
Herring .	120	4	
Kidney (raw) .	75	$2\frac{1}{2}$	Add $\frac{1}{2}$ oz. margarine.
Kipper .	112	$3\frac{3}{4}$	
Pork sausage (raw)	90	3	Omit $\frac{3}{4}$ oz. bread.
Spam .	90	3	

### EXCHANGES FOR ONE EGG

Calories—78

	Gm.	Approx. oz.	Remarks.
Bacon .	15	$\frac{1}{2}$	Raw.
Cold ham .	37	$1\frac{1}{4}$	Lean only.
Cod roe .	60	2	Steamed.
Cheese .	22	$\frac{3}{4}$	
Finnan haddock .	75	$2\frac{1}{2}$	
Kidney .	60	2	Raw.
Lean Meat .	30	1	Cooked.
Meat paste .	30	1	As purchased.
Sardines .	30	1	Tinned in oil.
Pilchards .	37	$1\frac{1}{4}$	Tinned in oil.
White fish .	90	3	Steamed.

## EXCHANGES FOR TWO AND THREE OZ. OF MEAT

	2 oz. cooked lean meat. Calories—150		3 oz. cooked lean meat. Calories—225		Remarks.
	Gm.	Approx. oz.	Gm.	Approx. oz.	
Chop mutton . . .	30	1	45	1½	Grilled. Fat and lean without bone.
Chicken or rabbit	90	3	135	4½	Cooked. Flesh only.
Cod roe . . .	75	2½	112	3¾	Fried. Add ¼ oz. marg.
Herring . . .	75	2½	112	3¾	Fried or pickled.
Liver . . .	90	3	135	4½	Steamed.
Pork . . .	50	1¾	75	2½	Leg roast.
Pork sausage	60	2	—	—	Raw. Omit ½ oz. bread.
Salmon (tinned) )	90	3	135	4½	Stewed.
Salmon (fresh) )	75	2½	112	3¾	
Sweetbread )	90	3	135	4½	
Tongue . . .	50	1¾	75	2½	
Tripe . . .	120	4	180	6	Boiled.
White fish . . .	120	4	180	6	Steamed. Add ¼ oz. marg.

## EXCHANGES FOR BREAD

Three water biscuits

Or 2 Rich Tea biscuits

„ 2 pieces ryvita

„ cooked potato—75 gm.=2½ oz.

=30 gm. or  
1 oz. bread.

„ rice, etc., dry weight—20 gm.=¾ oz.

„ Benger's Food, dry weight—20 gm.=¾ oz.

„ macaroni (boiled)—100 gm.=3½ oz.

„ orange or other 10 per cent. fruit—150 gm.=5 oz.

„ apple or other 15 per cent. fruit—100 gm.=3½ oz.

Cooked potato—100 gm.=3½ oz.

Or Kellogg's All-Bran—2 heaped tablespoonfuls=30 gm.

„ cornflakes—1 teacupful=25 gm.

=40 gm. or  
1½ oz. bread.

„ 4 tablespoonfuls thick porridge

„ bananas, or other 20 per cent. fruit—100 gm.=3½ oz.

**The Treatment of the Obese Diabetic.**—The mildly obese diabetic can be treated by the use of Diet II (p. 348), with the caloric intake appropriately reduced. This can be done very simply by stopping the breakfast bacon. In this way a reduction of approximately 220 calories can be made, and the 1,800 calorie diet containing 130 gm. of carbohydrate can be reduced to approximately 1,600 calories, which is often sufficient to bring a moderately obese diabetic to more normal proportions. Where gross obesity exists, and in those cases which prove recalcitrant to the above milder method of treatment, it is advisable to restrict the carbohydrate to 100 or 115 gm. and the calories to 1,000 or 1,200. Examples of such diets are given on pp. 387-390.

**Rationing.**—Special concessions were made to diabetics during the war regarding the allowances for meat, cheese, butter, margarine and milk.

The present allowances made to diabetics by the Ministry of Food, which are subject to alterations, are:—

Meat, 3 rations . . . . .	3s. 6d. worth weekly.
Cheese . . . . .	12 oz. „
Milk . . . . .	7 pts. „
Butter, 3 rations . . . . .	6 oz. „
Margarine, 3 rations . . . . .	12 oz. „

There is no extra allocation of bacon or eggs. For emergency use diabetics are advised to keep a stock of canned vegetables, oatcakes, ryvita or vita-weat, tinned sardines, salmon, tongue or corned beef. It should be realized that the fat value of margarine is the same as that of butter. When fruit is unobtainable the 3½ oz. of orange on the diet sheet can be exchanged for extra potato, 1½ oz., or for extra bread, ½ oz. Some raw vegetable should be taken daily if this exchange is made or a 50 mg. tablet of ascorbic acid.

### INSULIN TREATMENT

We have seen that insulin is required for those diabetics who, after a suitable trial on the test 1,500 calorie diet, continue to have glycosuria, and that insulin treatment should be instituted at once for those who, when first seen, are found to be underweight and to have acetone as well as sugar in the urine. In addition, we shall see that all cases of diabetic coma or pre-coma require insulin in large doses; that diabetic children invariably need it, as do all cases of diabetes before and after surgical operations and most cases complicated by infections or gangrene.

A number of mild diabetic patients, however, particularly the obese and the elderly, are able to do without insulin altogether and to keep “sugar-free” by attention to diet alone. The expense of insulin to the individual or the state, the inconvenience of its hypodermic administration, and the fact that its use is not entirely free from danger, makes it desirable to do without it whenever possible. The attempt to dispense with insulin, however, should never be pushed to the extent of depriving the individual of carbohydrate or calories sufficient to make his diet palatable, to keep him free from ketosis or to maintain him in a good state of nutrition.

Many patients are averse to start insulin and doctors hesitate to prescribe it in the belief that once started it will have to be continued for life. In a large percentage of cases this permanent administration is, of course, necessary. When this is so, delay in starting insulin is merely a matter of putting off the evil day, and in the meantime the patient will probably lose in condition, and his sugar tolerance will become progressively more and more impaired. Such a patient may, indeed, require eventually much larger doses than he would have done had insulin been given earlier. It is a fallacy, however, to suppose that insulin once started need in every case be permanently administered. After an initially severe hyperglycaemia has been well controlled by the use of insulin, it is often possible to reduce the dose and even to do without it altogether, the patient reacquiring much of his lost sugar tolerance. Again, insulin may be required as a temporary measure because of some superadded infection, but when this subsides the



sugar tolerance may once more improve so that the patient may be able to tolerate an adequate diet without the help of insulin.

**Technique of Injection.**—There are three kinds of insulin in common use: the original soluble insulin, zinc protamine (Z.P.) insulin and globin insulin. Soluble insulin is put up in strengths of 20, 40 and 80 units to the cubic centimetre. Z.P. and globin insulin are only issued in 40 and 80 unit strengths. The more concentrated preparations should be used when big doses are necessary so as to avoid the need for giving uncomfortably large subcutaneous injections.

It is very desirable that an insulin syringe graduated in units (20 divisions per cubic centimetre), rather than an ordinary 1 c.c. or minim syringe, should be used, especially when the patient is going to administer the drug himself. It is a more accurate method and saves mistakes in calculation. Most insulin syringes are graduated in 20 units per cubic centimetre. This should be made perfectly clear to a patient who is being given the 40 or 80 unit preparations. Thus if 16 units of 40-unit strength are prescribed, he should only take 8 according to the graduations on his syringe.

Practically all patients can and should be taught to administer insulin to themselves. This is of the utmost importance, as it makes the patient much more independent and saves an infinity of bother. A great deal of encouragement, a little mild bullying and most patient explanations are sometimes necessary to begin with. If this initial trouble is taken, it is only very little children, the senile, the blind and the half-witted who cannot be taught to administer the drug to themselves accurately and efficiently. Most patients in the course of time come to regard their daily injection, or injections, with no more seriousness than they do other routine duties such as brushing their teeth.

Cases of sepsis as the result of soluble and globin insulin injections are extremely rare, but zinc protamine insulin occasionally gives rise to subcutaneous abscesses in spite of the fact that aseptic precautions seem to have been taken at the injection. The patient should be taught to keep the needles in surgical spirit and to draw the syringe through with the spirit before use. Care should be taken to get rid of all the spirit from the needle and syringe before drawing in the insulin, as traces of surgical spirit in the injection will cause it to sting unpleasantly. Methylated spirit is often used instead of surgical spirit, the only drawback to it being that needles left in it for a long time tend to become rusty. Many patients keep their syringe with needle attached all ready for use in a portable metal case with a screw top containing surgical spirit. This is an excellent plan, and the initial expense is not great. We recommend our patients to boil their syringe once a week to ensure cleanliness.

When patients complain unduly of the pain of insulin injections, it is usually due to the fact that they are making the injections too superficially just under the skin. We have sometimes seen patients who had caused multiple necrotic areas in the skin as a result of making what were practically intradermal injections. The injection should be made quickly and resolutely with a sharp fine needle into the loose fatty subcutaneous tissues. The best places for self-injection are the outer surfaces of the thighs and the loose tissues of the abdomen (see p. 943). The site of the injection should be continually varied. Occasionally patients keep injecting themselves

in practically the same spot for weeks on end, causing thickening of the skin in that site with painful nodules in the underlying tissues and even, on occasion, large areas of fat atrophy. Occasionally red, tender urticarial wheals make their appearance at the site of the injection. Such reactions are not uncommon when Z.P. insulin is used, as they are due to sensitization to the protein fraction which it contains. When such local reactions do occur, they are usually only troublesome for a few days and tend to get less marked and to disappear entirely in the course of a week or a fortnight. Until spontaneous desensitization occurs, antihistamine drugs should be used (see p. 96) to prevent the reactions, which they do very effectively.

Soluble insulin should be injected half an hour before meals. This gives sufficient time for the insulin to begin to have its effect on the blood sugar in preparation for the meal, but not long enough to cause hypoglycæmic symptoms to develop before the meal is taken. Z.P. and globin insulin, which are only given once a day, should be injected as early as is conveniently possible before breakfast.

When soluble insulin has to be given in addition to Z.P. insulin it is injected first. The syringe is then disconnected from the needle, which is left sticking in the thigh, a new needle is fitted to the syringe and the dose of Z.P. insulin is sucked in. The syringe is then once more connected to the original needle and the Z.P. insulin is injected. Thus the two forms of insulin are not mixed in the syringe, but the patient only gives himself one prick with the needle. This technique has been adopted as experience has shown that it is difficult to measure accurately a dose taken from two rubber-capped vials into the same syringe, and also because a considerable proportion of the soluble insulin is converted into protamine insulin by coming into contact with it in the syringe.

**The Action of Soluble, Zinc Protamine and Globin Insulins.**—The healthy pancreas continually secretes a small amount of insulin to regulate endogenous metabolism. A meal, especially one rich in carbohydrate, causes a sudden temporary increase in this secretion to deal with the exogenous food intake. Thus the normal pancreas, so to speak, provides a constant service which it appropriately increases at rush hours. At present it is impossible to imitate perfectly this natural process of secretion by the injection of any of the available insulins.

*Ordinary or soluble insulin* has a rapid and powerful but transient action, having its maximum effect on the blood sugar in from two to four hours. This effect wears off within about six hours. Soluble insulin thus imitates only the emergency secretion of the normal pancreas which occurs in response to a meal. In a severe diabetic who has practically no endogenous supply of insulin of his own it is apparent that soluble insulin would have to be injected three times a day in order to control the blood sugar adequately. Even then some of the night hours are left unprovided with the essentials for the proper combustion of food, and some degree of hyperglycæmia is then almost unavoidable, since severe cases will break down some of their endogenous protein into carbohydrate. In addition, as the effect of the last injection of insulin wears off and carbohydrate metabolism diminishes, fat is also inefficiently metabolized and some degree of ketosis may result.

*Z.P. insulin* is prepared by combining protamine with insulin to form protamine insulin. A trace of zinc added to the insulin protamine mixture maintains the stability of the compound and helps to prolong its action.

When properly buffered this cloudy suspension is found to be sparingly soluble in tissue fluids, and when given hypodermically breaks down slowly, gradually releasing insulin which thus exerts a continuous mild effect on the blood sugar. Z.P. insulin has little effect for two or three hours after its injection. It then becomes gradually effective, and when a large dose has been given it may continue to have an appreciable action for twenty-six hours or more. It may still, therefore, be mildly effective at breakfast-time on the day subsequent to that of the injection. Its maximum action is usually observed in from eight to twelve hours, according to the size of the dose which has been given. The rapid fluctuations in the height of the blood sugar, which are noted after the injection of soluble insulin, are not observed with Z.P. insulin. It thus imitates the constant secretion by the normal pancreas, but its continuous gentle action is ill-suited to cope with the sudden strain of a high carbohydrate meal, especially one taken immediately after its injection.

*Globin insulin* is prepared by combining insulin with globin, a protein obtained from red blood cells after removal of the chromogen fraction. A clear solution is formed to which a trace of zinc is added. Its effect is maximal in from five to eight hours after injection, and is almost completely exhausted in eighteen hours. Its action is thus much slower and more prolonged than soluble insulin, but rather more rapid and transient than Z.P. insulin.

**Choice of Insulin.**—It is apparent from what has been said that soluble insulin is the drug for emergencies such as diabetic coma or pre-coma when a rapid therapeutic effect is essential. The blood sugar can be controlled quickly by its use, and, owing to the fact that its effect wears off rapidly, the subsequent doses may be varied according to the degree of glycosuria found. Thus in cases in which a patient's sugar tolerance is undergoing rapid alterations, or when, owing to intercurrent illness, the diet cannot be stabilized, soluble insulin provides an elastic method of treatment which can be adapted to the circumstances of the moment.

For the maintenance treatment of a stabilized case or when it is not a matter of urgency to bring a mild case under control, one of the depot insulins (Z.P. or globin) may be used. Their main advantage over soluble insulin lies in the fact that their use usually involves only a single injection a day. Further, Z.P. insulin controls the blood sugar during the night more efficiently than soluble insulin, as the effect from an injection of the latter given before the evening meal wears off by the early hours of the morning as may the effect of globin insulin given the preceding morning. It must be stressed, however, that depot insulins take a long time to bring a severe hyperglycæmia under control, and when ketosis is present they are extremely ineffective, so that a patient with ketonuria may sometimes relapse into diabetic coma in spite of the fact that he is taking a considerable daily dose of one of them. When patients are not under fairly constant medical supervision, or when they are notoriously careless about their diet, there is no question that they are safer to use soluble than depot insulins.

Under certain circumstances, as will be seen, soluble insulin may be combined with one of the depot insulins in treatment, advantage thereby being taken of the rapid action of the one and the prolonged action of the other. This combination is especially useful in the case of patients who readily excrete acetone in the urine, as experience shows that depot insulins are much less effective than soluble insulin in the control of ketosis.

**Control of a Severe Case by Insulin.**—When a patient with severe diabetes, having much sugar and acetone in the urine, first comes for treatment, insulin is started at once. No attempt is made to treat him by dietetic means alone. A diet slightly below that which will ultimately be required for maintenance is given. As it is important to get such a case under control as soon as possible, soluble rather than a depot insulin is used at first. The injections are made half an hour before breakfast and supper—the greater part of the carbohydrate for the day being given at these two meals. The initial dose will, of course, depend on the severity of the case. When no *very* great urgency exists an average dose will be 14 units in the morning and 14 in the evening. The patient is taught to test his own urine and to keep a chart of the result of the tests. The specimens to be tested are those passed (1) on rising in the morning, (2) before the midday meal, (3) before the evening meal, (4) before retiring at night. Glycosuria in samples (2) and (3) will call for an increase in the morning dose, while glycosuria in samples (4) and (1) will call for an increase in the evening dose. Daily increases of from 2 to 4 units per dose can be made according to the degree of glycosuria, though larger increases are necessary in urgent cases. In severe cases it may be found that the morning insulin does not control the hyperglycæmia in the afternoon, but that the dose cannot be further increased owing to the occurrence of hypoglycæmic symptoms before the midday meal. In such a condition the morning dose is somewhat reduced so as to abolish the midday hypoglycæmia, and a small dose of insulin can be given before the midday meal to abolish the glycosuria of the afternoon. When a midday dose is given a small reduction in the evening dose is often necessary. Owing to the transient action of soluble insulin a completely sugar-free urine in the early morning specimen is often unattainable in severe cases, but once glycosuria has been abolished during the day, or reduced to insignificance, conversion from soluble to one of the depot insulins should be undertaken.

The total dose of soluble insulin which has been found necessary during the day is noted. If this has been moderate—30 units or less—we prefer to use globin to Z.P. insulin. Being a clear solution rather than a cloudy suspension it is less variable in its rate of absorption, is less likely to give rise to local skin reactions and does not usually produce such intractable hypoglycæmic states. The previous total dose of soluble insulin gives the approximate amount of globin insulin likely to be required. This should be given in a single dose before breakfast. In subsequent days the dose may have to be gradually increased or decreased by two or four units at a time according to the urine tests. A moderate glycosuria in the morning specimen can be disregarded if good control is secured during the day.

If, however, the case has been sufficiently severe to necessitate a large total dose of soluble insulin, conversion to a mixture of Z.P. and soluble insulin is the method of choice, as a sufficient dose of globin insulin cannot be given to control sugar metabolism during the night hours without causing hypoglycæmia during the day. Soluble insulin is used along with Z.P. insulin in order to prevent the hyperglycæmia which would otherwise occur after breakfast before the slow acting Z.P. insulin begins to be effective. Some two-thirds of the total dose of soluble insulin is given as Z.P. insulin and the other third as soluble insulin. For example, if a total dose of 45 units of soluble insulin has proved necessary to stabilize a case, 30 units of Z.P. insulin plus 15 units of soluble insulin should be used as the initial

dose on conversion. The quick action of the soluble insulin will prove effective for some hours after the injection, by which time the slower acting Z.P. insulin will have come into play. In succeeding days it is often possible to reduce and eventually to abandon altogether the soluble insulin. If necessary the dose of Z.P. insulin is appropriately increased as the other is withdrawn. In severe cases, however, it is often impossible to give a dose of Z.P. insulin big enough to ensure absence of hyperglycæmia throughout the twenty-four hours without inducing hypoglycæmia some time during the day or night. In such cases a small dose of soluble insulin has to be retained to deal with the hyperglycæmia induced by breakfast, the dose of Z.P. insulin being appropriately reduced to avoid hypoglycæmic symptoms in the evening or at night. As a general rule it is unwise for the practitioner to attempt to control a case with an injection of more than 40 units of Z.P. insulin alone. If the patient's midday urine still contains sugar after such a dose, it is wise to supplement it with soluble insulin rather than to go on increasing the dose of Z.P. insulin still further. If the evening and morning specimens still contain sugar as well, the dose of Z.P. insulin may be increased in addition.

It is necessary to see patients frequently while conversion from soluble to a depot insulin is being undertaken. In individual cases the previous total dose of soluble insulin is only approximately equal to the amount of depot insulin which will be required.

Once hyperglycæmia has been satisfactorily controlled it is often possible gradually to reduce the dose of insulin in the succeeding weeks, as the patient's sugar tolerance usually improves under proper treatment. This improvement is often striking.

Slight modifications have to be made in the diet when a patient is changed from soluble to a depot insulin. If, for instance, he is taking soluble insulin night and morning most of the carbohydrate would be given at breakfast and at supper and as little as possible at the other meals unprotected by insulin. When the same patient is given globin insulin the main carbohydrate meals should be at midday and at 4.30 P.M., for globin insulin has not become very effective at breakfast-time and its effect tends to wear off in the late evening. When Z.P. insulin alone is being used the main carbohydrate meals should be tea and supper with a snack before going to bed at night so as to prevent nocturnal hypoglycæmia. If a mixture of Z.P. and soluble insulin is being given the carbohydrate should be evenly distributed over the day. These are only approximate rules, however, and may have to be modified in individual cases, since the optimum spacing of the carbohydrate in any given case can often only be discovered by trial and error. If it is found, for instance, that a patient persistently shows a tendency to become hypoglycæmic at a certain time and yet to have glycosuria at other times an appropriate shifting of the carbohydrate can be made from one meal to another to obviate these effects.

When reasonable control of a patient's glycosuria has been established the urine tests need only be made on the early morning and night specimens; and when thorough stabilization has been achieved the occasional testing of a twenty-four-hour specimen is all that is necessary.

**Control of a Moderate Case by Insulin.**—A new case of diabetes which has been found to require insulin can be started on globin insulin, provided the diabetic condition is not severe and no significant degree of ketosis is present.

It takes longer to control a case by this method, which is, however, simpler as no conversion from one insulin to another is involved. Twelve or 14 units can be given to begin with, and this dose can be increased appropriately by 4 units at a time until reasonable control is established. Unless the patient is under close observation in hospital it is wise to allow three or four days to elapse between each increase in dose.

Although globin insulin is our insulin of choice for the control of moderate cases, there are undoubtedly some which do better on Z.P. insulin, and if difficulty is experienced in stabilizing a case satisfactorily on the one there should be no hesitation in making a trial of the other. Occasionally a case is found which is refractory to both depot insulins. Such patients complain that they never feel well while receiving the depot insulin and, in spite of careful control of the diet, fluctuate between a marked hyperglycæmia at certain times of the day and a tendency to hypoglycæmia at others. In these cases it may be necessary to revert to two doses of soluble insulin. It should again be stressed that patients who are careless about their diet, who because of their occupation have to have meals at irregular intervals, or who are likely to be out of reach of skilled medical advice for long periods of time, are safer on two doses of soluble insulin than on one of the depot varieties.

**Hypoglycæmia.**—An overdose of insulin results in an undue lowering of the blood sugar causing the symptoms of hypoglycæmia to manifest themselves. The degree to which the blood sugar must fall to produce hypoglycæmic symptoms varies considerably. In a normal healthy individual a blood-sugar concentration of as low as 60 to 70 mg. per cent. is usually necessary to produce symptoms. In the diabetic, however, who has become accustomed to a high blood sugar, hypoglycæmic symptoms may occur at considerably higher concentrations. The level at which it occurs seems, indeed, to depend roughly on the average height of the blood sugar previously. Thus, when a severe diabetic, who has had a high blood sugar continuously for some time, first comes under treatment and has his hyperglycæmia rapidly controlled, hypoglycæmic symptoms may occur when his blood-sugar concentration is still as high or even higher than 120 mg. per cent. Later on, after his tissues have become accustomed to a more normal blood sugar, hypoglycæmic symptoms may not occur unless the blood-sugar concentration falls to 60 or 70 mg. per cent.

Hypoglycæmia due to soluble insulin usually begins with a feeling of weakness and emptiness about the pit of the stomach. Tremor and tachycardia are common and diplopia occasionally occurs. The individual feels faint and dizzy and often experiences a strong desire for food. Clammy sweating is almost invariable, and, as the condition becomes more pronounced, mental symptoms are common, the patient sometimes becoming very hysterical—laughing, crying, shouting and struggling. Some most respectable diabetics, while hypoglycæmic, have run amuck in the streets and have been apprehended by the police as drunk and disorderly. At other times lassitude and somnolence are more marked features, especially in the case of children. The advanced stages of hypoglycæmia are characterized by muscular twitchings, deepening coma and eventually by convulsions.

Reactions with depot insulins, particularly Z.P. insulin, are more severe than with soluble insulin and more difficult to treat, the patients tending to slip back again into coma after they have been brought out of it, unless

large amounts of glucose are given. Further, the reactions may differ symptomatically from those due to soluble insulin. Many of the symptoms of soluble insulin hypoglycæmia are due to endogenous adrenaline which is secreted in an attempt to raise the blood sugar. In consequence sweating, palpitation and tremors are its characteristic features. Hypoglycæmia produced by Z.P. insulin, on the other hand, comes on so slowly that this outpouring of endogenous adrenaline does not occur to the same extent, and general malaise, nausea and headache are the symptoms most commonly experienced—sweating, palpitation and tremor being less marked. Z.P. insulin hypoglycæmia may also give rise to intractable vomiting, which may be prolonged after the blood sugar has returned to normal or even to hyperglycæmic levels. A starvation ketosis may therefore be added to the ordinary diabetic tendency to ketosis and the original hypoglycæmic reaction may gradually merge into a true diabetic coma. In our view this is a not infrequent cause of diabetic coma nowadays and is insufficiently realized. It constitutes a further drawback to the use of Z.P. insulin. Patients should be warned of these novel features of hypoglycæmia before being given depot insulins, since failure to recognize the symptoms as being due to hypoglycæmia may prevent them from taking appropriate measures and a severe hypoglycæmic coma may ensue. Reactions with Z.P. insulin may occur at any time during the twenty-four hours, but are more frequent in the latter part of the day and at night than during the morning, while those due to globin insulin are most likely to take place from midday to 4 P.M. Hypoglycæmia from soluble insulin usually takes place within four hours of the injection.

The more severe hypoglycæmic symptoms seldom manifest themselves for at least a quarter of an hour after the initial sensations have been experienced. Thus, the patient has usually plenty of time to rectify matters. The treatment consists, of course, in raising the blood sugar by the administration of carbohydrate. This can be done most conveniently and simply by expediting the next meal, for in this way there is no disturbance of the patient's carbohydrate and calorie intake for the day. Hypoglycæmia does not, however, invariably occur under circumstances in which a meal can be taken. All patients, therefore, who are taking insulin should invariably carry about with them some lumps of sugar. After taking sugar the patient should remain as quiet as possible till the symptoms have disappeared, as exercise tends to exacerbate the tendency to hypoglycæmia. A drink of water should be taken with the sugar in order to facilitate its rapid absorption. If the symptoms do not quickly disappear, or should they become worse, another two lumps of sugar can be taken or, preferably, 10 gm. of glucose. The object should be to banish the symptoms with the smallest effective quantity of sugar in order not to disturb unduly the sugar intake for the day and to cause hyperglycæmia and glycosuria. When sugar is not at hand, as it always should be, any other carbohydrate food—such as orange juice or bread—can be taken. The latter, however, being more slowly absorbed, is less effective in dealing with the emergency of hypoglycæmia than sugar or orange juice.

In the great majority of cases these measures are rapidly effective. Occasionally, however, a patient with severe hypoglycæmia is encountered in deep coma and unable to swallow. In such circumstances a subcutaneous injection of  $\frac{1}{2}$  c.c. of adrenaline (solution 1 : 1,000) should be given. This converts any available glycogen into glucose, thereby raising the blood sugar.



This procedure is usually effective in rousing the patient from his coma sufficiently to permit him to swallow carbohydrate food, which should be given, if possible, in the form of glucose or sugar in orange juice. An intravenous injection of 100 to 200 c.c. of 10 per cent. glucose solution, or the giving of 2 oz. of glucose in 10 oz. of water by stomach tube, are measures which are seldom necessary, but may occasionally have to be resorted to in exceptionally severe cases. The giving of rectal glucose salines, which is sometimes advocated, is a very slow and uncertain method of raising the blood sugar and is not to be recommended in such emergencies.

All patients taking insulin should have the symptoms of hypoglycæmia carefully explained to them, and should be thoroughly conversant with the necessary treatment. Some careless patients who do not take their disease sufficiently seriously may have to have the dangers of hypoglycæmia stressed to them. We believe, however, that many doctors overstress the dangers of hypoglycæmia, causing their patients to become unduly alarmed about it. This exaggerated terror of hypoglycæmia is responsible for much insufficient dosage, or even for insulin administration being withheld or stopped, with disastrous consequences. Thus the slightest, and often imaginary, feelings of discomfort are sometimes made the excuse by the patient for a debauch on sugar; or again, if some gastric upset renders a patient temporarily unfit for his ordinary diet, insulin is often discontinued altogether from fear of hypoglycæmia. This is one of the most fruitful causes of diabetic coma. When a patient becomes unfit for his ordinary food a light fluid diet should be substituted (see pp. 379, 382), and if necessary the ordinary dose of insulin may be appropriately reduced, but should never be discontinued as long as sugar is present in the urine. When the digestion is upset as the result of an infection, the insulin requirements should be increased rather than diminished. It should always be remembered that while the number of deaths from diabetic coma are legion, those from hypoglycæmia are so rare as to be clinical curiosities.

Hypoglycæmia may be due to a natural improvement in the patient's sugar tolerance, to the fact that he has missed or been too late in taking his meal or that he has taken too little of it. When it is simply due to the dose of insulin being excessive, this should be reduced on the succeeding day by 2 or 4 units, depending on the severity of the symptoms, or alternatively the carbohydrate in the diet may be appropriately increased where this is desirable. Exercise enables a diabetic to do with less insulin than when he is leading a sedentary existence, and unusual physical exertion is a common cause of hypoglycæmia. When soluble insulin is being taken, the dose immediately prior to strenuous exercise should be slightly reduced, but with depot insulins it is wiser to eat a little more carbohydrate prior to such exercise rather than to reduce the morning dose.

### SPONTANEOUS HYPOGLYCÆMIA

This condition may be considered conveniently here, though it is, of course, the direct opposite of diabetes mellitus. Many normal people, during prolonged and hard exercise on an empty stomach, experience mild hypoglycæmic symptoms, such as slight faintness, sweating and a curious pathological sensation of hunger. This is probably simply due to the fact that they are very plentifully endowed with active islet tissue in the pan-



creas, and such people learn to carry a biscuit or some sweets with them to eat when they are taking strenuous exercise for long periods.

Symptoms of hypoglycæmia are not uncommon in patients who have had a subtotal gastrectomy and are usually experienced about an hour and a half after a high carbohydrate meal. The gastric remnant empties itself very rapidly into the jejunum from which sugar is quickly absorbed. This results in a transient hyperglycæmia and a reactive hyperinsulinism causing a brisk fall in blood-sugar concentration, sometimes to hypoglycæmic levels.

Very rarely patients are encountered in whom "physiological hypoglycæmia" is exaggerated into severe hypoglycæmic attacks in which actual coma may even develop. In such cases a marked diffuse hyperplasia of islet tissue may be present.

The uncommon condition of localized adenoma of the pancreatic islet tissue—either simple or malignant—may result in repeated attacks of hypoglycæmic coma, with blood-sugar levels of well below 40 mg. per cent. These attacks of unconsciousness may sometimes be prolonged for many hours. It is difficult without an exploratory laparotomy to distinguish between spontaneous hypoglycæmic coma, the result of diffuse hypertrophy of islet tissue, and that due to a localized pancreatic adenoma. In the former case nothing can be done surgically apart from the very drastic procedure of resecting a portion of the pancreas; in the latter complete cure results if the adenoma can be discovered and successfully removed. All cases in whom repeated attacks of unconsciousness are found to be associated with blood-sugar concentrations of under 40 mg. per cent. should be advised to undergo laparotomy in the hope that an adenoma can be discovered and extirpated. Even when it is present this may be a complicated procedure, as the tumour may be very small and difficult to differentiate from the normal pancreatic tissue.

When operation is contraindicated or refused or when no adenoma can be found the only treatment is to advise frequent meals and the avoidance as far as possible of strenuous exercise, particularly on an empty stomach. The attack itself should be treated in the same way as ordinary insulin hypoglycæmia (see above) and the patient should always carry sugar in some form to take whenever the sensations of hypoglycæmia begin to be experienced. At first sight it might appear natural to recommend that the diet should be of a high carbohydrate content, but such feeding stimulates hyperinsulinism and increases the frequency of the attacks. Experience suggests that the frequent feeds are better to be of a good mixed character, but tending to be high in fat rather than in carbohydrate. Ephedrine in  $\frac{1}{2}$ -gr. doses (30 mg.) three times a day between meals is sometimes of value.

#### THE USE OF BLOOD-SUGAR TESTS IN TREATMENT

It is commonly believed that diabetes mellitus cannot be treated satisfactorily without the use of blood-sugar examinations. We believe, contrary to many authorities, that practically all the information required for treating the *average* case efficiently may be obtained by frequent urine examinations without undertaking examinations of the blood, which are distasteful to the patient, frequently impracticable outside an institution or large centre, and which, in our opinion, need only be resorted to in certain circumstances. The method of examining twenty-four-hour specimens,

and, when necessary, each specimen of urine passed, until the suitable diet—and possibly the suitable dose of insulin—for the patient has been established, has a wide application. Any reasonably intelligent patient, after he has been taught to test his urine by Fehling's method, can make the necessary observations for himself. Nor do we think it necessary to estimate the amount of sugar passed in the urine by quantitative methods. It is held by some that in this way the amount of insulin required can be accurately calculated on the principle that 1 unit of insulin looks after 2 gm. of glucose. In practice, however, this is such a very approximate statement that with experience the dose of insulin can be gauged just as accurately by the condition of the patient and the result of the Fehling test—whether brown, yellow, green, or blue. Once the diet and the insulin dosage suitable for the patient have been established by the method of frequent examinations of the urine, the testing of an occasional night and morning urine specimen with an occasional test of a twenty-four-hour specimen, is sufficient for practical purposes.

The objection to the method of controlling dietetic and insulin therapy by analysis of the urine alone lies in the fact that it yields information only that the blood sugar is below or above the renal threshold of the patient. In diabetics this threshold may occasionally be raised very considerably, so that a significant hyperglycæmia may exist without any sugar being present in the urine. We have repeatedly observed, for example, in old-standing diabetics, fasting blood-sugar values of between 200 and 300 mg. per 100 c.c. without glycosuria being present. It has not yet been definitely established whether hyperglycæmia, moderate enough to show no glycosuria, should be treated as a matter of great significance. Some workers believe that it should, holding that any degree of hyperglycæmia may cause further retrogression of sugar tolerance, and that it may be a factor in producing the arterial degenerations so common in the senile type of diabetic. On the other hand, it is possible that in diabetes of long standing the organs and tissues have become acclimatized to working at their optimal efficiency with a slightly higher blood-sugar level than normal, and that this hyperglycæmia may not, therefore, be entirely harmful. Certainly in many cases an attempt to keep the blood sugar of an old-standing diabetic within strictly normal limits causes, as we have seen, hypoglycæmic symptoms to occur, and the patient feels less well than when a moderate hyperglycæmia, though without glycosuria, is allowed to persist. Though occasional blood-sugar examinations may be ideal, we believe that for all practical purposes the diet and insulin should be so regulated that sugar does not appear in significant quantities in the urine, and that the treatment of the average case can be carried out perfectly satisfactorily by examination of the urine alone.

One of the exceptions to this rule is to be found in the case of a true diabetic with a low renal threshold for sugar. Such cases, which are quite common, especially during pregnancy, are most difficult to treat, since any attempt to keep the urine entirely free from sugar is usually followed by hypoglycæmic symptoms. In such cases, therefore, glycosuria may occur even when the blood sugar is perfectly normal, and efficient treatment cannot be conducted by urine analysis alone, but demands occasional blood-sugar estimations as well. These estimations should be carried out on the early morning fasting blood, which gives an indication as to the adequacy of the evening dose of soluble insulin or of the depot insulin given on the previous

morning, and on a specimen of blood taken four hours after the morning dose, at which time the effect of the morning soluble insulin should be maximal. The tests should be done once every two months, or more often while the case is being stabilized. A blood-sugar concentration of under 150 mg. per cent. should be looked upon as perfectly satisfactory. Higher figures suggest that the preceding doses of insulin can be increased.

When a patient is taking a depot insulin it may occasionally be difficult to determine whether symptoms of malaise and headache are due to hypoglycæmia or to general causes. Under such circumstances a blood-sugar test is often useful.

### THE TREATMENT OF DIABETIC COMA

Diabetic coma is practically always preventable, and should never occur when an intelligent patient is under efficient treatment. Occasionally it may be encountered in an undiagnosed untreated case; sometimes it is due to simple disregard of treatment by the patient or to grossly ineffective treatment on the part of the doctor; more often it is the result of gastro-intestinal upsets, infections or surgical operations in diabetics who are being adequately treated for all ordinary occasions but whose treatment is insufficiently elastic to cope with such emergencies.

Diabetic coma is a medical emergency which demands the constant attendance and care of the physician. In severe cases it requires skilled nursing and technical assistance, which are not easily procured outside hospital. It is a condition in which expert treatment may make all the difference between the life and death of the patient. In the majority of severe cases, therefore, when skilled institutional treatment can be procured, the patient should be transferred to hospital after first-aid treatment in the form of an adequate injection of insulin has been given by the practitioner.

The principles of treatment in diabetic coma are to eradicate the ketosis by giving soluble insulin, and to combat the invariable dehydration and circulatory collapse by giving fluids. In addition, it is wise to wash out the stomach when vomiting is occurring; to clear the bowel when constipation is present, which is usually the case; and to search for and—when present—to evacuate pus, or to treat any associated infection which may have been the original cause of the coma.

**Insulin.**—It is insufficiently appreciated that diabetic coma requires a very large quantity of insulin for its successful treatment. Further, the insulin should be used in large doses in the first few hours of treatment rather than in moderate amounts spread over twenty-four hours. Soluble insulin should invariably be used, since Z.P. and globin insulin, owing to their slow action, are entirely unsuited to cope with the emergency of diabetic coma. From 500 to 700 units, or even more, may have to be administered in the twenty-four hours to patients in severe diabetic coma, but the major portion of this should be given in the first few hours of treatment. Thus from 75 to 100 units should be given as an initial dose, depending on the severity of the case, 30 to 50 of which can be given intravenously, as the absorption of insulin from the subcutaneous tissues may, in a severe case, be very slow owing to the shocked state of the patient. A further 50 to 100 units should be given subcutaneously an hour and a half, and three hours, later. Thus from 175 to 300 units, depending on the severity of the case, should be injected in the first three hours of treatment. Thereafter

appropriately smaller doses with longer intervals between them can be administered till the ketosis has been satisfactorily controlled.

Too often quite insufficient doses of insulin are administered in this emergency from fear of inducing hypoglycæmia. There is little danger of this in the early stages, and it is unnecessary and even undesirable to "cover" these initial doses with glucose, which used to be thought such an essential part of the treatment. It is true that the body as a whole is depleted of sugar in diabetic coma, though the blood sugar is high, and, theoretically, comparatively small doses of insulin ought to be sufficient to lower the blood sugar to hypoglycæmic levels unless adequate covering doses of glucose are given at once. In practice, however, a patient in diabetic coma is extremely resistant to insulin, and in the early stages of treatment large doses can be given freely without much danger of the patient slipping imperceptibly from the coma of ketosis to that of hypoglycæmia, provided the urine is tested prior to each injection and a large quantity of sugar is found to be present. The object to be aimed at is a rapid diminution of the ketonuria with a slower decrease of the glycosuria. It is, of course, ideal to have in addition frequent estimations of the blood sugar. When this is possible the dose of insulin may be gauged with greater accuracy.

**Fluid.**—All patients in diabetic coma are profoundly dehydrated owing to the polyuria which has always preceded the condition, and to the vomiting with which it is so often associated. Evidence of this dehydration is to be found in the dry skin, leathery tongue, high blood urea and collapsed veins of the patient, and in the profound fall in blood pressure and intra-ocular pressure which also occur. The treatment of this dehydration and its associated circulatory collapse is almost as important as the treatment of the ketosis itself, but is often forgotten or treated inadequately.

When the patient can swallow and retain fluid, large quantities of water should be given by the mouth and frequent drinks of hot tea and coffee. The retention of such fluids is often made possible by an initial gastric lavage, preferably with a weak solution of bicarbonate of soda. Even in mild cases it is desirable and in severe cases essential to augment the fluid intake by an intravenous drip transfusion. Two litres of normal saline should be administered by this method in the first three hours of treatment. If the patient is still dehydrated at the end of this time and unable to swallow or retain fluids adequately, then the transfusion must be continued. This extra fluid, however, should be given in the form of six per cent. glucose, without saline, owing to the danger of producing hyperchloræmia, and to the fact that by this time the blood-sugar concentration may be falling significantly under the influence of the large doses of insulin which have been administered. The veins of patients in deep diabetic coma are unfortunately so collapsed that it may occasionally be impossible to administer transfusions without cutting down upon one of them and inserting a cannula. The rectal administration of fluids is a most unsatisfactory substitute for intravenous drip transfusion and is not to be recommended in this emergency.

**Diet.**—After the first three hours of intensive treatment by insulin and fluid the patient will usually have recovered sufficiently to permit of oral feeding, which should be started as soon as possible. 25 gm. of glucose in solution, or equivalent feeds of common carbohydrate foodstuffs (see p. 378), should be given every two hours until the patient is fit for a more ordinary diet. It should be remembered in selecting the appropriate food that strong sugar solutions

are apt to cause vomiting, and, when this is a feature of the case, it is better to give—instead of glucose or ordinary sugar—feeds of Benger's Food.

When the patient is so far recovered as to be able to eat more ordinary food, a light diet, as described on p. 379, can be given for a day or two with appropriate doses of soluble insulin three or four times a day. The same sort of diet will be found suitable for cases of diabetic ketosis in danger of coma and for diabetics temporarily unfit to take their ordinary diet owing to gastro-intestinal upsets or intercurrent infections. As long as the ketonuria is controlled, no serious attempt need be made at this stage to get the patient "sugar free" till he is again fit to take his normal diet.

Owing to the toxic effect of severe diabetic ketosis on the circulatory system, patients recovering from diabetic coma should remain in bed till their resting pulse rate has become normal. This may take a week or more in many cases.

### DIABETES IN CHILDREN

Diabetes may occur at any age, but it is relatively uncommon in children, especially in young children. This is fortunate, for the treatment of the diabetic child is much more difficult than that of the adult for a variety of reasons. It is impossible, for example, to stabilize a child for long on a standard diet and a fixed dose of insulin as it is often possible to do in the case of an adult, for his nutritional needs are continually altering according to his changing development.

To provide for his growth and energy requirements, a child needs relatively higher diets than an adult in respect of protein, carbohydrate and total calories, and a generous supply of milk must be given. A high fat intake, however, especially in young children, is often poorly tolerated, producing ketosis and fatty stools, and large quantities of green vegetables are often insufficiently digested. Further, just as a child's temperature is notoriously unstable, so his sugar tolerance is more variable from day to day than that of an adult. This may be accounted for to some extent by the uncontrolled temper of children and by the great variation in their physical activity from day to day. Thus the passionate tears, the transports of joy, the wild excitements and intense activities, which characterize the life of children, have profound temporary effects on their sugar tolerance. Insulin itself often acts more acutely in children than in adults, producing an unusually rapid fall in the blood-sugar level to be succeeded by an equally rapid rebound. Again, children are more liable to infectious diseases than adults, and infections, as we have seen, are the bugbear of diabetics. Lastly, few children suffer from mild diabetes, but usually from an acute type of the disease, showing a marked tendency to ketosis. For these reasons insulin is an invariable necessity for child diabetics who cannot tolerate without its help diets adequate to furnish energy for their activities and to permit of normal growth. To deprive such children of an adequate diet in the hope of doing without insulin simply leads to their taking illicit food surreptitiously, or to retarding their physical and mental development and predisposing them to infections such as tuberculosis.

The difficulties in treating diabetes in children are, however, by no means insurmountable, and with the help of insulin and wise dietetics there is no reason why they should not live a normal life and grow into strong





and healthy adults. It is important to take the child himself into the doctor's and parent's councils, to treat him as an intelligent person and to give him a sense of responsibility in regard to his own health. Children respond well to such treatment and frequently become the best diabetic patients. Parents, indeed, may be to some extent comforted by the assurance that the self-control and discipline inculcated by their child's training in good diabetic habits will stand him in good stead in the future.

**Calories.**—In prescribing the calories for the diabetic child there are various aspects which must be kept constantly in mind. An excessive caloric intake is always harmful from the diabetic standpoint no matter whether the calories are derived from carbohydrate, protein or fat. On the other hand, the child must have sufficient food to satisfy his appetite, to meet his requirements for energy and to allow for growth. The diet must be regularly adjusted to meet these needs, since a normal rate of growth and increase in weight should be aimed at. Unfortunately, stunted growth in a diabetic child cannot always be remedied by additions to the diet, for it is often endocrine in origin. Some diabetic children, on the other hand, are abnormally tall for their age, and this point must be taken into account when considering their caloric requirements. Other diabetic children tend to become unnaturally fat, especially if they are taking large doses of insulin, and overfeeding has to be carefully guarded against in such cases. It will be seen, therefore, that age is not the only criterion as to the child's caloric requirements, but it is a useful guide.

By consulting Table I (a) and (b) it can be ascertained if a child is approximately the average weight for his height and age, and, unless he is very abnormal, he may safely be given one of the standard diets described below. In constructing these diets we have chosen the lower rather than the higher caloric standards (except in the case of the younger children), for many children will be of smaller build than the standard we have taken, and, moreover, the urine can be cleared of sugar at this lower level and if necessary the diet can then be increased. The diabetic child usually thrives on a number of calories rather below the usual intake of a healthy child. Children of the same age vary considerably in their capacity for food and it is impossible to gauge the appetite exactly. When fixing the child's theoretical requirements it is safest to base the calculation according to the *standard* weight rather than the actual weight for height and age. This will avoid overfeeding the short fat child and underfeeding the tall lean one.

**Protein.**—It is obvious that adequate protein is extremely important for children of all ages and any attempt to keep the diabetic child on a minimum allowance is to be deprecated. An unnecessarily high protein intake is also undesirable since it will lessen the tolerance for carbohydrate, and, in children especially, large quantities of meat increase the tendency to acidosis.

Table II shows the amount of protein believed to be advisable for the normal child. Slight deviations from this standard are immaterial.

**Carbohydrate.**—The benefit derived from a reduction in carbohydrate in the diabetic diet has already been discussed and the undesirability of too low an intake has been emphasized. The same principles apply to the treatment of the child diabetic, but a relatively higher carbohydrate allowance is desirable. This is required to allow for the necessary pint of milk (which is responsible for 30 gm. of carbohydrate), and, moreover, high fat and low carbohydrate diets are unsuitable for young children.



TABLE II

Age (Years).	Calories per Kilogram Body-weight.*	Grammes of Protein per Kilogram Body-weight.†
1	90 to 100	3.5
2		
3		
4	80 to 90	3.0
5		
6		
7	70 to 80	2.5
8		
9		
10	Girls, 60 to 70 Boys, 65 to 75	2.0
11		
12		
13	Girls, 40 to 60 Boys, 50 to 65	1.5
14		
15		
16		
17		
18		

\* From Rose's "Laboratory Handbook for Dietetics."

† From the Report on the Physiological Basis of Nutrition drawn up by the Technical Commission of the Health Committee of the League of Nations.

Under modern treatment the diabetic child receives an adequate amount of fruit, bread and potato, though in our opinion it is advisable to avoid actual sugar and jam, for once a child has forgotten the taste of sugar he is less likely to indulge in sweets. The omission of sugar may be one of the factors responsible for the unusually sound teeth possessed by many young diabetics.

Most diabetic children are now given about 150 gm. of carbohydrate daily. Children under five years of age are usually satisfied with less, while those of over ten may need considerably more. The hungry child might be allowed extra vegetable, but care must be taken not to cause gastro-intestinal over-distension or irritation.

**Fat.**—Excessive amounts of fat are undesirable from a digestive point of view and also because of the tendency to ketosis which is common in children. On the other hand, the really low fat and high carbohydrate diets sometimes used in the treatment of adult diabetics are quite unsuitable. Such diets are badly balanced for children and predispose to infections. The quantity of fat given in the standard diets for the younger children is very similar to that eaten by the normal child, while the allowance for the older children is somewhat higher.

**Minerals and Vitamins.**—It is very important that the diabetic child should have a generous supply of minerals and vitamins to provide for growth and to build up his resistance to infection. The calcium, phosphorus and iron content of the standard diets are all adequate, but children should be encouraged to eat extra cheese in place of eggs or bacon occasionally in order to improve the calcium intake. A helping of fish may be given twice a week in place of meat or eggs. The allowance of vegetable, fresh fruit, milk, eggs and whole grains in the standard diet provides all the necessary vitamins, except that during the spring and winter months cod-liver oil or

one of the concentrated preparations of vitamin D (or A and D) is advisable.

The child should be encouraged to drink water freely; this will help to prevent constipation and it is especially necessary if there is a tendency to acidosis.

The carbohydrate in the sample diets given is more or less evenly distributed over the four meals. This is suitable when zinc protamine insulin is being used, but if soluble insulin is given twice daily the carbohydrate should be redistributed.

DIETS FOR DIABETIC CHILDREN (Table showing the Three Main Diets)

	Age.	3 Per Cent. Veg.	10 Per Cent. Fruit.	Potato.	Bread.	*Porridge.	Milk.	Bacon	No. of Eggs.	Meat.	Cheese.	Butter or Marg.	C.	P.	F.	Cals.
		Gm. Oz.	Gm. Oz.	Gm. Oz.	Gm. Oz.	Tablesp.	C.c. Pt	Gm. Oz.		Gm. Oz.	Gm. Oz.	Gm. Oz.	Gm.	Gm.	Gm.	
Diet I	Three or four years	150 5	180 6	75 2½	105 3½	3	600 1	30 1	1 1	30 1	..	22 ½	135	56	71	1403
Diet II	Seven or eight years	150 5	180 6	90 3	120 4	4	600 1	45 1½	1 1	45 1½	22 ½	45 1½	150	70	107	1843
Diet III	Eleven or twelve years	300 10	120 4	100 3½	135 4½	4	600 1	45 1½	2 2	75 2½	22 ½	75 2½	160	86	144	2280

\* Thirty grams (1 oz.) dry oatmeal makes approximately 4 tablespoonfuls porridge.

† In war-time use exchanges for eggs and fruit (see p. 353).

For intermediate ages, see Notes for suitable additions.

### DIET I

#### TYPE OF DIABETIC DIET FOR CHILD AGED TWO TO FIVE YEARS

*Child of Three or Four Years.*—Carbohydrate, 135 gm. Protein, 56 gm. Fat, 71 gm. Calories, 1,318.

##### Breakfast—

Bacon, 30 gm.—1 oz.

Brown bread, 15 gm.—½ oz.

Porridge, 3 tablespoonfuls.

Butter, 7 gm.—¼ oz.

Milk, 150 c.c.—5 oz.

##### Dinner—

Clear soup or marmite if desired.

3 per cent. vegetable (see Group I, p. 350), an average helping.

Potato, 75 gm.—2½ oz.

Cooked lean meat, 30 gm.—1 oz.

\*Milk, 150 c.c.—5 oz.

10 per cent. fruit, 90 gm.—3 oz.

##### Tea—

Tomato and lettuce as desired.

Brown bread, 45 gm.—1½ oz.

1 egg.

Butter, 7 gm.—¼ oz.

Milk, 150 c.c.—5 oz.

##### Supper—

Brown bread, 45 gm.—1½ oz.

Butter, 8 gm.—¼ oz.

10 per cent. fruit, 90 gm.—3 oz.

(or exchanges).

Milk, 150 c.c.—5 oz.

To increase this diet for *child of five years*:—

	Carb.	Prot.	Fat.	Cals.
Add Cheese, 15 gm.—½ oz.	..	4	4.5	56
Butter, 7 gm.—¼ oz.	..	..	6	54
..	..	4	10.5	110

Total: Carbohydrate, 135 gm. Protein, 60 gm. Fat, 80 gm. Calories, 1,500.

\* The milk may be used for curds or a custard can be made using 100 c.c. of milk and half an egg from tea. The other half-egg can be exchanged for ½ oz. of grated cheese. Milk jelly can be made with a small teaspoonful of gelatin and flavoured with saccharin and coffee, vanilla, etc. Bacon can be exchanged for one egg+10 gm. (½ oz.) butter.

## DIET II

## TYPE OF DIET FOR CHILD OF SIX TO TEN YEARS

*Child of Seven or Eight Years.*—Carbohydrate, 150 gm. Protein, 70 gm. Fat, 107 gm. Calories, 1,843.

*Breakfast—*

Bacon, 45 gm.—1½ oz.	Milk, 150 c.c.—5 oz.
Brown bread, 30 gm.—1 oz.	Butter, 10 gm.—½ oz.
Porridge, 4 tablespoonfuls.	

*Dinner—*

Clear soup or marmite if desired.	Butter, 10 gm.—½ oz.
3 per cent. vegetable (see Group I, p. 350), an average helping.	Milk, 150 c.c.—5 oz. for curds or custard using an egg from another meal.
Cooked lean meat, 45 gm.—1½ oz.	10 per cent. fruit, 90 gm.—3 oz., or extra potato, 45 gm.—1½ oz.
Potato, 90 gm.—3 oz.	

*Tea—*

Tomato and lettuce as desired.	Brown bread, 45 gm.—1½ oz.
	Butter, 15 gm.—½ oz.
1 egg	
Cheese, 22 gm. } or exchanges for 2 eggs (see p. 351).	
Egg may be transferred to another meal.	Milk, 150 c.c.—5 oz.

*Supper—*

10 per cent. fruit, 90 gm.—3 oz., or extra bread, 18 gm.—¾ oz.	Butter, 10 gm.—½ oz.
Brown bread, 45 gm.—1½ oz.	Milk may be omitted at dinner and extra given at supper.
Milk, 150 c.c.—5 oz.	

To reduce this diet for *child of six years*:—

	Carb.	Prot.	Fat.	Cals.
<i>Omit</i> Butter, 10 gm. . . . .	..	..	8·5	76
Cheese, 22 gm., or sometimes 1 egg	..	6	6	78
	<u>0</u>	<u>6</u>	<u>14·5</u>	<u>154</u>

Total: Carbohydrate, 150 gm. Protein, 64 gm. Fat, 93 gm. Calories, 1,613.

To increase diet for *child of ten years*:—

	Carb.	Prot.	Fat.	Cals.
<i>Add</i> Meat, 15 gm. . . . .	..	4	2·5	39
Bread, 15 gm. . . . .	7·5	1·5	0·25	38
Butter, 15 gm., or thick cream, 30 c.c. . .	..	..	12·5	112
	<u>7·5</u>	<u>5·5</u>	<u>15·25</u>	<u>189</u>

Total: Carbohydrate, 157 gm. Protein, 75 gm. Fat, 122 gm. Calories, 2,026.

If hungry, a little extra vegetable can be given.

## DIET III

## TYPE OF DIET FOR CHILD OF ELEVEN TO TWELVE YEARS

\* *Child of Eleven or Twelve Years.*—Carbohydrate, 160 gm. Protein, 86 gm. Fat, 144 gm. Calories, 2,280.

*Breakfast—*

Bacon, 45 gm.—1½ oz., and 1 egg (or exchange).	Porridge, 4 tablespoonfuls.
Butter from ration (use some for frying).	Brown bread, 30 gm.—1 oz. Milk, 100 c.c.—3½ oz. Weak tea.

*Dinner—*

Clear soup or marmite if desired.	Cooked lean meat, 75 gm.—2½ oz.
3 per cent. vegetable (see Group I, p. 350), a large helping.	10 per cent. fruit, 120 gm. (or ex- changes, see p. 351).
Potato, 100 gm.—3½ oz.	Milk, 150 c.c.—5 oz. for curds or custard using egg from another meal.
Butter from ration.	

*Tea—*

Tomato and lettuce as desired.	Cheese, 22 gm.
Brown bread, 60 gm.—2 oz.	Butter from ration.
	Weak tea, with milk, 100 c.c.

*Supper—*

Vegetable as at dinner.	(If preferred, replace 20 gm. of bread by 100 gm. of 10 per cent. fruit.)
1 egg (or exchanges).	Butter from ration.
Brown bread, 45 gm.—1½ oz.	Milk, 250 c.c.—one glass.

Daily butter ration, 75 gm.

If afforded, replace 15 gm. of butter by 30 c.c. of thick cream—2 tablespoonfuls.

Any of the following additions could be made according to the patient's appetite and the calories required.

	Carb.	Prot.	Fat.	Cals.
Meat, 15 gm.	..	4	2.5	39
Bread, 20 gm.	10	2	..	48
Bacon, 15 gm.	..	2.5	7	73
Cheese, 15 gm.	..	4	5	61
Milk, 300 c.c.	15	10	12	208

For children of fourteen years some or all of the above additions may be made to Diet III. If preferred, the diets for adults (see p. 348) may be used.

\* This diet will satisfy many diabetic children of twelve years, but the calories are below theoretical requirement and may have to be increased to satisfy the appetite or to maintain satisfactory weight. Unnecessarily high diets should be avoided.

Those containing 160 or 200 gm. of carbohydrate should be selected and an additional  $\frac{1}{4}$  pint of milk must be included, giving calories suitable to the individual child.

### DIABETES AND PREGNANCY

As the result of insulin and modern dietetic treatment the amenorrhœa and sterility so common in diabetics in pre-insulin times have been greatly diminished, and pregnancy is much more common in diabetic women than used to be the case, though they are still less fertile when compared to non-diabetic women of similar age. The practitioner may be consulted as to the desirability of his diabetic patients becoming pregnant, and where the woman already has two or three healthy children a further pregnancy should be discouraged. There is always a slightly increased risk for the woman herself; her diabetes may become temporarily and sometimes permanently more severe; she is much more liable to hydramnios and has a greater tendency to toxæmia than normal women. The foetal and neo-natal mortality is greatly increased in diabetes, and even in clinics where the mother is carefully treated from the diabetic point of view it may not be far short of 50 per cent. This increased mortality is principally due to the greatly increased liability of diabetic women to develop toxæmia of pregnancy. A subsidiary cause may be found in the fact that the foetus may become unduly large as the result of the excessive quantities of sugar it receives from the maternal blood. It thus matures too early and at normal term may be post-mature and insufficiently viable to withstand the prolonged labour which its size may entail. Rarely a fatal spontaneous hypoglycæmia may occur in the newly-born child, as hyperplasia of the foetal islets of Langerhans sometimes takes place in response to the maternal hyperglycæmia. Death of the foetus in utero or during the neo-natal period from no obvious cause is very common. Lastly, there is a hereditary tendency in diabetes, and when a diabetic history is also present on the paternal side pregnancy is inadvisable for this reason alone. The maternal, foetal and hereditary risks, however, are not such as to justify the practitioner from advising against pregnancy in a diabetic woman with no children or only one, who is really anxious to have a family and who is ready to be co-operative in treatment, provided there is no diabetic history on the paternal side of the family.

Diabetes may develop during pregnancy in women who have not previously suffered from the disease, but glycosuria at this time is seldom due to true diabetes. A blood-sugar curve is always advisable, and if this shows a mere lowering of the renal threshold for sugar, no special diet is indicated. Such patients should, however, be watched carefully, as occasionally—though the blood-sugar level is normal—so much sugar is passed in the urine that ketosis may develop. In such a case a normal diet suitable for pregnancy should be given along with sufficient insulin to prevent ketosis. No attempt should be made to keep the urine free of sugar, since hypoglycæmia would be the result.

The presence of lactose in the urine will give a positive reaction for sugar, and should be differentiated from glucose by suitable tests. Lactose may appear during the later months of pregnancy and during lactation, and its presence is of no importance.

A few cases of true diabetes developing for the first time during pregnancy clear up completely during the puerperium. At this time it is important to be on the lookout for hypoglycæmia, as the sugar tolerance sometimes returns to normal with startling rapidity after delivery. The blood-sugar curve should be repeated during the puerperium to make sure that the diabetic tendency has disappeared. Such cases should be watched carefully during subsequent pregnancies.

During pregnancy the carbohydrate tolerance will fluctuate and the insulin must be regulated accordingly. The renal threshold for sugar is usually lowered in pregnancy so that control of the diabetic state by urine tests may not prove entirely satisfactory and occasional blood-sugar estimations may be necessary (see p. 362). The insulin requirement is usually considerably increased from the fourth or fifth month onwards, and it may fall significantly after delivery. In some cases there is an improvement in carbohydrate tolerance during the last month, so that hypoglycæmia must be watched for at this stage. It is thus essential that the patient should be seen at frequent intervals throughout the pregnancy.

As foetal mortality is chiefly due to the increased tendency of diabetic women to develop toxæmia of pregnancy, a careful watch should be kept for early signs of the condition. The blood pressure should be noted frequently and the urine should of course be examined for albumin as well as for sugar and acetone. A sudden increase in weight should be viewed with suspicion, for œdema may occur even in the absence of albuminuria. Excess of salt should be avoided during pregnancy, especially in the presence of œdema. Constipation should be guarded against and the diet should be regulated to avoid it. Bran will be found useful in these cases.

The work of Smith and Smith has suggested that in many diabetic pregnancies there is an increase of gonadotrophin excretion and a fall in œstrogen and pregnanediol excretion. They claim that toxæmia of pregnancy, and hence foetal mortality in diabetics, is very greatly decreased by œstrogen therapy. Very large doses of stilbœstrol are recommended—starting at the 16th week of pregnancy, 30 mg. should be given daily, and this dose should be increased by 5 mg. each week. This work, however, has still to be generally confirmed.

In order to avoid an excessively large post-mature foetus involving a prolonged and difficult labour, Joslin and his associates, and also R. D. Lawrence, recommend a Cæsarean section for a first pregnancy between the 36th and 38th weeks, and this is wise advice. Alternatively, ordinary labour may be induced artificially at the 36th or 37th week.

As spontaneous hypoglycæmia occasionally occurs in the infant of a diabetic mother during its first twenty-four hours of life, three-hourly feeds of a small teaspoonful of sugar in two ounces of water should be given during this time.

If a diabetic woman is in good condition she should be encouraged to attempt to nurse her child, at least during the first month or two. If she does so, it must be remembered that she will require a liberal diet of approximately 3,000 calories. It must be confessed, however, that it is exceptional for diabetic mothers to have a sufficient supply of milk to undertake successful lactation.

The *dietary* requirements during pregnancy are rather similar to those of the growing child—protein, minerals and vitamins being of the utmost

importance. Little or no increase in calories is required during the first four months of pregnancy, though the diet should be modified to include a pint of milk.

After four months an increase of 10 to 20 per cent. in calories may be needed, but the diabetic, being used to a low caloric intake, seldom requires as many calories as the normal pregnant woman. Overfeeding is most undesirable, but patients who usually take 1,800 calories may need 2,200 during pregnancy, or those previously on 2,000 calories may require from 2,300 to 2,400.

The protein requirement during pregnancy is said to be about 1.5 gm. per kg. of body-weight. About 90 gm. is usually included in the diet, but this does not entail eating large quantities of meat since the necessary milk will provide the extra protein. Not less than 1 pint—preferably  $1\frac{1}{2}$  pints—of milk should be included and cheese should also be taken to ensure an adequate calcium intake. The carbohydrate should not be less than 175 gm.; it may well be increased later in pregnancy, since the foetus may demand some 50 gm. of carbohydrate during the last two months of pregnancy. Fat will make up the remaining calories, but some women tolerate fat poorly during pregnancy, especially during the early months, and it may often be necessary to increase the carbohydrate and to lower the fat.

The diet should be a well-balanced one with a generous supply of "protective foods." Iron may be required in medicinal form (see p. 470), and a preparation of vitamins A and D is essential, especially during the spring and winter months (see p. 970), as well as orange juice.

The standard diet given below should be modified to suit the individual patient, but it will serve as a useful guide. Lower fat, and therefore lower caloric diets, are desirable for the patient with a tendency to obesity or an intolerance for much fat. Insulin is required in all but the mildest cases.

#### DIET FOR PREGNANCY

##### (Latter Half)

Cho. 200 gm. P. 98 gm. F. 129 gm. Cals. 2,353

##### *Breakfast—*

Porridge, 6 tablespoonfuls or exchange.

Bacon,  $1\frac{1}{2}$  oz. or exchange (see p. 351).

Bread,  $1\frac{1}{2}$  oz.

Tea or coffee.

Milk and butter from allowance.

##### 11 a.m.—

Glass of milk from allowance.

##### *Dinner—*

Clear soup, bovril or marmite, if desired. (Avoid if flatulence troublesome.)

Cooked lean meat, 2 oz. or exchange (see p. 352).

Vegetable from Group I, large helping, or vegetable from Group II, 1 tablespoonful (see p. 350).

Potato, 3 oz.

Orange,  $3\frac{1}{2}$  oz. or exchange (see p. 351).

Milk from allowance as curds, or coffee or to drink.

*Tea—*

Salad of vegetable from Group I, if desired.

Bread, 2 oz.

Cheese,  $\frac{3}{4}$  oz. now or at any other meal.

*Supper—*

Cooked lean meat, 2 oz. or exchange (see p. 352).

Vegetable as at dinner, if desired.

Orange,  $3\frac{1}{2}$  oz. or exchange (see p. 351).

Bread, 2 oz.

Tea or coffee with milk from allowance.

Butter from allowance.

*Daily*—Milk,  $1\frac{1}{2}$  pints; Butter or margarine,  $1\frac{1}{2}$  oz.

*N.B.*—To reduce calories omit one of the following:—

	Calories.
Margarine, 15 gm.— $\frac{1}{2}$ oz. . . . .	112
Bacon, 15 gm.— $\frac{1}{2}$ oz. . . . .	77
Meat, 30 gm.—1 oz. . . . .	77

If necessary, add or deduct 1 oz. bread. Cho. 15. Cals. 77.

### COMPLICATIONS OF DIABETES

**Tuberculosis and Diabetes.**—The liability of severe diabetics to develop tuberculosis should constantly be kept in mind. The possibility of this complication having occurred should always be suspected and excluded when, for no obvious reason, a previously well-controlled diabetic begins to require larger doses of insulin, to lose weight and to fail in general health. The danger is particularly present in patients who have suffered from diabetic coma and in diabetic children. Such cases should be examined at intervals for the specific purpose of excluding tuberculosis; young diabetic patients particularly should be kept from association with open cases of tuberculosis.

With early diagnosis of the tuberculosis and efficient treatment of the diabetes, our experience does not suggest that the prognosis is unduly gloomy or that the diabetes has an adverse effect on the tuberculous process. A considerably higher calorie diet should be given to such cases than to the average diabetic.

**Gangrene.**—A large number of cases of diabetic gangrene can be prevented by cleanliness, proper care of the feet and immediate treatment of the slightest abrasion of the feet which may occur. Diabetic gangrene is exceedingly rare under the age of forty. Its frequency advances as age increases, just as it does in non-diabetic gangrene.

The first maxim in the prevention of gangrene is cleanliness. Joslin has said that if diabetics kept their feet as clean as their faces gangrene would be practically unknown. Elderly diabetics should therefore be encouraged to wash their feet night and morning with soap and water, to dry them thoroughly and to powder them afterwards. Warm socks, or stockings, should be worn and easy-fitting soft leather shoes. New shoes should only be worn for a few hours a day until they are broken in. Bed socks should be used instead of hot-water bottles. All corns and callosities should be treated with the greatest care, if possible by a competent chiropodist who



should be warned that the patient has diabetes. Abrasions of the skin should not be dressed with strong antiseptics such as iodine, but with a simple spirit solution. The toe nails should be carefully cut in a good light, and any overlapping toes should be kept separate by inserting cotton-wool between them.

The treatment of obliterative vascular disease and gangrene is discussed on p. 687.

**Neuritis, Retinitis, Cataract, Pruritus.**—The adequate control of the underlying diabetic condition itself is the best treatment for the neuritis, retinitis and pruritus with which diabetes is so commonly associated. These complications frequently improve when the glycosuria is controlled. True diabetic peripheral neuritis is much less common than is often supposed. The pains in the legs so often complained of by elderly diabetics are more often due to vascular causes. Pain due to diabetic neuritis is somewhat similar to the lightning pains of tabes. Apart from the administration of analgesics such as codeine and aspirin, rigid control of the diabetic condition is the only treatment of any value. A generous diet should be given, as most of these patients are thin and tend to improve as weight is regained, though the condition is often extremely intractable. Vitamin B is of no service in this type of neuritis.

Many diabetics on first coming under treatment complain of a blurring of vision which is the result of a rapid lowering of a high blood sugar to normal. They may be reassured that this symptom will disappear once the eyes have become habituated to the new conditions.

Failure of vision, the result of diabetic retinitis, is not greatly relieved by the prescription of glasses. Some patients suffering from diabetes waste a great deal of money in having their spectacles frequently changed, since what suits them on one day is often found to be unsuitable a few days later. The acuity of vision tends to vary from day to day depending on the adequacy of the diabetic control. The onset of cataract demands a consultation with an ophthalmologist as to the feasibility of operative treatment and as to the correct time for its performance.

Pruritus usually clears up rapidly with the disappearance of glycosuria. Its treatment when it persists is discussed on p. 184.

**The Adjustment of the Diet in Complications.**—The average diabetic diet is unsuitable in cases of gastro-intestinal disturbances or in acute infections, since it is usually bulky and high in residue and may contain considerable amounts of fat and fried foods. No attempt must be made to force unsuitable standard diets upon a patient unable to digest or to enjoy them.

The fluid feeds and the light diets given on pp. 378, 379, 382 will be found suitable in many cases. It is impossible, however, to give detailed dietetic directions to suit all possible contingencies, and when diabetes is complicated by other diseases which make the standard diets unsuitable the practitioner will often be well advised to obtain the advice of a specialist.

**Peptic Ulcer.**—A diabetic may develop a peptic ulcer and there is no reason why the two conditions should not be treated satisfactorily at the same time. An ulcer régime can be given containing a definite amount of carbohydrate and calories. In such cases about 175 to 200 gm. of carbohydrate are necessary to allow for milk to be given between meals and to include fine cereals and orange juice. Protein should be higher than usual (ideally about 100 to 120 gm.) to permit of sufficient eggs, fish, finely divided meat

and milk being taken. The amount of fat will depend upon the calories required, but unless the patient is overweight, cream and butter are desirable from the ulcer standpoint. Sugar should be omitted, fruit and vegetables must be sieved, while white bread, and later fine brown bread, should take the place of coarse cereals. Fried and highly seasoned foods, meat soups and strong tea and coffee should be omitted. The meals should be small and frequent.

*Cardiac Disease.*—In cardiac cases, or for any patients with flatulence, bulky vegetables should be omitted, fluids should be given between meals only, and crisp toast should replace bread. Only a light supper is indicated. Diabetic patients showing signs of œdema should curtail their salt intake.

*Diarrhœa.*—Diarrhœa is sometimes troublesome, especially in elderly diabetics, and irritant purgatives should never be given to those patients. When an attack of diarrhœa occurs the fat in the diet should be reduced and the fruit and vegetables and the coarse cereals should be omitted temporarily. The carbohydrate should be increased by the addition of boiled milk, fine cereals and crisp toast. Symptoms of hypoglycæmia must be watched for in these cases. Should the diarrhœa become chronic, care must be taken to give adequate vitamins, and a colitis diet may be necessary (e.g., low residue, low fat, moderate carbohydrate and high protein (see p. 578)).

*Fevers.*—In cases of acute illness such as influenza, pneumonia or any septic condition, the patient may develop ketosis rapidly and pass into diabetic coma if prompt treatment is not given. In such cases the treatment already described for impending diabetic coma may be necessary (see p. 364), but if the doctor is summoned in time less drastic doses of insulin may suffice. In the event of a severe cold, fever, sickness, abdominal pain or any infection, the diabetic should be warned to stay in bed and to call in the doctor.

Patients who are taking insulin must on no account omit it even if they cannot take their usual food. They are advised to divide the usual dose or doses into three or four smaller doses. It has already been mentioned that soluble insulin is more suitable than Z.P. or globin insulin in emergency work, though a small dose of one of the depot insulins can be given in addition before breakfast. In acute diseases three or four doses of soluble insulin will be required daily and the increase in total insulin requirement may be considerable even though the diet is curtailed. If severe vomiting is present, hospital treatment is essential since intravenous glucose will be needed. In the case of patients who live far from a doctor it is advisable to give them a note of suitable feeds to be taken in times of emergency (see pp. 378, 379).

In all cases of fever and acute illness the diet should be mainly fluid, and the feeds given below and on p. 382 should be administered with due regard to the patient's preferences. About 100 to 120 gm. of carbohydrate should be included daily; this will be given in four feeds, each feed being preceded by soluble insulin. Diluted milk, unsweetened orange juice, weak tea, chicken tea and bovril can be given between meals (reckoning the carbohydrate of the milk and orange juice). Water should be taken very freely. When the acute stage is over, the light diet on p. 379 should be given and thereafter the patient's usual diet should be gradually resumed.

## FLUID FEEDS

(Each feed contains approximately 25 gm. carbohydrate)

	Carb.	Prot.	Fat.
Benger's Food, dry weight, $\frac{1}{2}$ oz.—15 gm. . . . .	12	1.5	0
Milk, 6 oz.—180 c.c. . . . .	9	6	7
Sugar, 1 teaspoonful—5 gm. . . . .	5	0	0
	26	7.5	7
Orange juice, $3\frac{1}{2}$ oz.—100 c.c. . . . .	10	0	0
Glucose, $\frac{1}{2}$ oz.—15 gm. . . . .	15	0	0
Squeeze of lemon juice or lemon flavouring. . . . .	..	..	..
	25	0	0
Strained porridge, 4 tablespoonfuls . . . . .	20	5	2
Milk, $3\frac{1}{2}$ oz.—100 c.c. . . . .	5	3.3	4
	25	8.3	6
Bread, $\frac{3}{4}$ oz.—22 gm. . . . .	12	2	0
Milk, 6 oz.—180 c.c. . . . .	9	6	7
Sugar, 1 teaspoonful—5 gm. . . . .	5	0	0
	26	8	7
Ovaltine, $\frac{1}{3}$ oz.—10 gm. . . . .	7	1.5	1
Milk, 8 oz.—240 c.c. . . . .	12	8	9.5
Sugar, 1 teaspoonful—5 gm. . . . .	5	0	0
	24	9.5	10.5
Horlick's, $\frac{1}{2}$ oz.—15 gm. . . . .	11	3	1.4
Milk, 8 oz.—240 c.c. . . . .	12	8	9.5
Sugar, $\frac{1}{2}$ teaspoonful—3 gm. . . . .	3	0	0
	26	11	11

## LIGHT DIABETIC DIET

Cho. 145 gm. P. 60 gm. F. 77 gm. Cals. 1,513

*Breakfast—*

Strained porridge, 4 tablespoonfuls or exchange (see p. 352).

Bread, 1 oz. (crisply toasted).

Diabetic marmalade, if desired.

Tea or coffee.

Milk and butter from allowance.

11 *a.m.*—

Glass of milk or white coffee made with milk from allowance. 1 tea biscuit.

*Dinner—*

Chicken, rabbit or any lean tender meat, 2 oz. or exchange (see p. 352).

Purée'd vegetable, 1 tablespoonful.

Potato, 2 oz.

Milk pudding made with  $\frac{1}{2}$  oz. cereal and milk from allowance.

Stewed apple,  $3\frac{1}{2}$  oz. Or orange,  $3\frac{1}{2}$  oz. or exchange (see p. 351).

*Tea—*

Bread, 1 oz. given as sandwich, if desired, using tomato, cress, lettuce or marmite.

Tea.

Milk and butter from allowance.

*Supper—*

1 egg lightly cooked or exchange (see p. 351).

Bread,  $1\frac{1}{2}$  oz.

Tea.

Milk and butter from allowance.

*Daily*—Butter or margarine,  $1\frac{1}{4}$  oz. ; Milk, 1 pint.

The total calories of this diet are low and it is only suitable for temporary use.

In place of cereal pudding at dinner-time a milk soup may be given using 1 small teaspoonful flour.

1 small teaspoonful margarine from allowance.

Milk from allowance.

1 tablespoonful purée'd tomato, carrot or spinach.

Stock or marmite may be added.

Or cereal may be omitted and  $\frac{1}{2}$  oz. bread added.

## THE CARE OF THE SURGICAL DIABETIC

The discovery of insulin and the introduction of various anæsthetics as substitutes for chloroform and ether have greatly lessened the dangers of surgery in diabetes. Nevertheless, the risk of an operation is still considerable if the patient falls into inexperienced hands. Successful treatment

depends upon close co-operation between the surgeon and the physician, and, if possible, a nurse who is experienced in the care of diabetic patients should be employed.

The chief danger in diabetic surgery is ketosis, which may be caused by giving an unsuitable anæsthetic, by prolonged starvation, by vomiting or by failure to control the glycosuria and blood sugar with sufficient insulin either before or after the operation. The routine measure of testing every patient's urine before operation is an obvious necessity, since it may be too late to give adequate treatment if the diabetes is only discovered after the operation. A general anæsthetic, especially chloroform, is well known to be toxic to the liver and has a tendency to cause some degree of ketosis even in the normal individual. This danger is greatly increased in diabetics owing to the poor store of glycogen in the liver, hence the necessity for giving glucose covered by an adequate dose of insulin *prior* to administering an anæsthetic.

Chloroform should never be given to a known diabetic, and ether should also be avoided if possible. Gas and oxygen, pentothal or a spinal or local anæsthetic are suitable from the point of view of the diabetes. Even with a well-chosen anæsthetic, sickness may occur after operation, and if this is prolonged dehydration will follow, thus increasing the dangers of ketosis and collapse from shock.

When the patient is taking fluids by the mouth sickness is sometimes caused by giving too strong a solution of glucose or by giving orange juice to patients who cannot tolerate it. In cases of severe vomiting a definite amount of glucose is administered by the intravenous route and a suitable insulin dosage must be given.

Apart from the hyperglycæmia which occurs after a general anæsthetic, the nervous shock which is inevitable in any operation tends to raise the blood sugar and to cause a return of glycosuria. In the presence of sepsis the carbohydrate tolerance is still further diminished and the insulin requirement is considerably increased until the infection subsides. As the patient recovers the decrease in insulin requirement is often marked, and care should be taken to ensure that hypoglycæmia does not occur at this stage.

In surgical cases it is too often assumed that the diabetes is the cause of all unusual signs and symptoms, and that drowsiness is necessarily due to ketosis, or that symptoms of collapse are always caused by an overdose of insulin. In a well-managed case these emergencies seldom occur. It should be remembered that the toxæmia caused by a large carbuncle or a severe gangrene is very great and may in itself result in drowsiness, while the senile diabetic with marked arterial degeneration may readily collapse from cardiac failure or go into coma as the result of a cerebral hæmorrhage.

It is neither desirable nor possible to outline a routine to be followed in all cases of diabetic surgery. Experience is the only sure guide to treatment. The method of preparing the patient will vary according to whether the operation is undertaken as an emergency measure or if there is time to prepare for some days beforehand, and the treatment must be modified to suit the surgical condition. The severity of the diabetes, the presence or absence of ketonuria and the choice of an anæsthetic are decisive factors governing insulin dosage. The advisability of operation cannot be discussed here, but all severe infections should be dealt with as soon as possible without waiting to clear up the glycosuria.

In cases which are not surgical emergencies the patient is stabilized for several days on a satisfactory diet, insulin being given if necessary. The carbohydrate of the daily diet should not be less than 145 gm. and preferably more should be given. The urine should be free from acetone and no appreciable amount of glycosuria should be present.

On the day of operation 30 gm. of carbohydrate should be given in the form of glucose in lemon, orange or grapefruit juice three hours before operation; sickness at the time of operation may occur if this is given one and a half to two hours before operation as is sometimes advocated. The dose of insulin will depend upon the patient's usual insulin requirement. In a mild case not previously requiring insulin, 10 units of soluble insulin may be enough; 15 units is a fairly common dose, but in more severe diabetics accustomed to larger doses of insulin, 20 to 30 units may be required, and in such cases 40 gm. of carbohydrate may be necessary. It is essential to use soluble rather than Z.P. or globin insulin as the latter cannot be adjusted from hour to hour. Further, the depot insulins are much less potent in controlling ketosis.

If the operation takes place in the morning the patient may feel inclined for a cup of tea with a lump of sugar (5 gm.) in the late afternoon, depending upon what anæsthetic he has had. In the evening a fluid feed of 25 gm. of carbohydrate (see p. 378) can usually be taken (unless this is contraindicated by the nature of the operation). Patients are often tired of glucose and orange juice and prefer Benger's Food. This feed is preceded by insulin as before, but rather a smaller dose should be given, especially if a specimen of urine can be obtained and is found to be "sugar-free." If sickness occurs, it will be necessary to administer the glucose intravenously. If the nature of the operation makes feeding by the mouth impossible or inadvisable, a measured quantity of glucose is usually given by the continuous-drip method and small doses of insulin will be required at regular and stated intervals, the quantity given depending upon the degree of glycosuria found to be present.

When there is no ketosis and the patient has been well stabilized before operation there is no necessity to give more glucose and insulin during the subsequent night, but in the case of an emergency operation on a diabetic with acetonuria more intensive treatment is required, as in impending coma. In such cases there may be no time to give glucose by the mouth before operation, and subcutaneous insulin and intravenous glucose should be given in the theatre and repeated later by the continuous-intravenous method until the acetonuria is controlled.

When only a local anæsthetic is given, as in diabetic cataract or for minor operations, the patient is allowed a light breakfast prior to operation, *e.g.*, tea, toast and butter and grapefruit or orange juice. If he has not been taking insulin previously it is unnecessary to administer it unless glycosuria is present. If the usual diet can be taken after operation a patient on insulin will have his customary dose.

Whenever the usual number of calories are not given, insulin must be reduced even though the usual carbohydrate allowance is prescribed. The diet for a case of cataract must be served in such a form that little mastication is necessary until the patient is discharged from hospital. It is important that serious glycosuria should be controlled, but any risk of insulin reaction must be avoided or the eye may be damaged during a hypoglycæmic fit.

## FLUID POST-OPERATIVE DIET

(Also suitable for patient recovering from Diabetic Coma)

	Carb.	Prot.	Fat.
<i>Early Morning—</i>			
Cup of tea; milk, 2 tablespoonfuls—30 c.c. . . . .	1.5	1	1
<i>Soluble Insulin, 7.30 a.m.</i>			
<i>Breakfast, 8 a.m.—</i>			
Strained porridge, 4 tablespoonfuls=dry meal, 1 oz.—30 gm. . . . .	20	5	2
Hot milk, 5 oz.—150 c.c. . . . .	7.5	5	6
<i>10.30 a.m.—</i>			
Milk, hot or cold, 5 oz.—150 c.c. . . . .	7.5	5	6
<i>Soluble Insulin, 12.30 p.m.</i>			
<i>Dinner, 1 p.m.—</i>			
Milk Soup:			
Milk, 4 oz.—120 c.c. . . . .	6	4	5
Sieved carrot, 1½ oz.—45 gm. . . . .	2.7	0.6	0
Or Tomato juice, 3 oz.—90 c.c. Stock or bovril, as required.			
Milk pudding:			
Dry cereal, ½ oz.—10 gm. . . . .	8	1	0
Milk, 6 oz.—180 c.c. . . . .	9	6	7
Milk to serve, 2 oz.—60 c.c. . . . .	3	2	2.4
<i>Tea, 4 p.m.—</i>			
Tea, with milk, 1 oz.—30 c.c. . . . .	1.5	1	1
One tea biscuit; or ½ oz. thin bread with butter to cover . . . . .	7	0.6	1
<i>Soluble Insulin, 6.30 p.m.</i>			
<i>Supper, 7 p.m.—</i>			
Benger's Food, ½ oz.—15 gm. . . . .	12	1.5	0
Milk, 6½ oz.—200 c.c. . . . .	10	6.6	8
Sugar, 1 teaspoonful—5 gm. . . . .	5	0	0
<i>9 p.m.—*</i>			
*Orange juice, 3 oz.—90 c.c. . . . .	9	0	0
Sugar, 1 teaspoonful—5 gm. . . . .	5	0	0
<b>Total . . . . .</b>	<b>115</b>	<b>39</b>	<b>39</b>
<b>Total Calories, 967.</b>			
* When orange juice is not available substitute:—			
Milk, 6 oz.—180 c.c. . . . .	9	6	7
Horlick's, 1 tablespoonful—8 gm. . . . .	5	1.5	0.7

Post-operative treatment will depend upon the individual case, but after an amputation of a leg, for example, the diet described on p. 382 would be suitable for the day after operation, the subsequent diet being built up on the lines of the light diet given on p. 379, until the patient is taking his usual diabetic diet.

## OBESITY

### INTRODUCTION

Up to the beginning of this century corpulence was on the whole regarded as a desirable and healthy attribute, and it has only been comparatively recently that medical interest has been focused on the more serious aspects of excessive weight. Quite apart from æsthetic considerations, long-continued obesity has as its almost invariable concomitants more or less grave disturbances of most of the systems of the body. Thus the statistics of Life Assurance Companies all go to show that mortality rates rise steadily in proportion to the extent to which people are overweight. Flat foot, varicose veins, osteo-arthritis of the knees and hips, postural backache, ventral herniæ, cholecystitis and gall-stones, diabetes, degenerative changes in and overstrain of the myocardium, angina pectoris, hypertension and bronchitis are all evils to which the corpulent are heirs more often than the lean. It is far too often forgotten that the more specific treatment of these ailments is likely to be unsuccessful if the associated obesity is allowed to continue. Indeed, reduction in weight is sometimes the only treatment required to banish the symptoms arising from the milder forms of such conditions.

Just as the maintenance of a constant body temperature under widely varying exogenous and endogenous conditions forms a striking fact of human physiology, so the maintenance by the healthy adult of an almost constant body-weight over long periods of time is a remarkable phenomenon, when it is remembered that this constancy may be maintained in spite of great variations in physical activity and food intake. The glutton does not necessarily become overweight, nor is the ascetic necessarily emaciated. It is certain that most of us eat in excess of our calorific requirements, but this excess, in the normal person, may not be absorbed or is easily burnt up and dissipated in the form of heat. Did this capacity not exist obesity would be almost universal, for a daily intake of 200 calories in excess of actual requirements, such as would be represented by an extra glass of milk or two slices of bread, would have the result of increasing the weight by some 24 lb. a year; and this is actually what may occur to some extent in certain unfortunate individuals in whom the mechanism for regulating body-weight is less flexible than in the normal person. On the other hand, some individuals become obese simply because they put their regulating mechanism to a strain which no ordinary mechanism is capable of withstanding.

Two types of obesity have, therefore, been distinguished: an exogenous type involving some dietetic error or some environmental factor, such as lack of exercise; and an endogenous type involving an abnormality of the weight-regulating mechanism, which is usually taken as synonymous with some endocrine disturbance. In practice it is impossible to make such an arbitrary



and clear-cut distinction in the majority of cases. The two extremes are obvious enough: on the one hand, there are cases showing the typical stigmata of endocrine deficiency; on the other hand, there is the individual who has habitually sacrificed his figure to his appetite and his indolence. In between these two extremes, however, lie the great majority of cases which are hardly susceptible of classification into one or other type. It is probable that in these latter no single factor is responsible, but rather a mixture of mild exogenous factors combined with some small degree of endocrine upset, the exact nature of which may be as yet unrecognizable by the means at our disposal.

As far as the treatment of obesity is concerned it is usually unnecessary to distinguish between endogenous and exogenous obesity since both types respond to the same therapeutic methods. In each case income exceeds expenditure and rational therapy must consist in correcting the balance. Further storage may be prevented by cutting down the intake of food, or by causing more rapid metabolism so that the stores of fat may be depleted. Dieting has long been recognized as a successful method of treatment and many régimes have been recommended. An increased combustion of food-stuffs can be encouraged in two ways: by increasing physical effort; or by raising the general level of metabolism. In popular imagination lack of exercise bulks large as a cause of obesity, and hard exercise is looked upon as a specific weight reducer. Severe and sustained muscular work is, however, necessary if any significant increase in the expenditure of calories is to be attained. This will be appreciated when it is recalled that a man of average size only consumes about 60 extra calories while walking a mile on the level, and very often increases his appetite thereby to the extent of adding several hundred calories to his subsequent meal. Further, owing to the disabling effects of obesity it is rarely possible for a fat person to take really hard physical exercise. The alternative to exercise is to employ hormone or drug therapy to influence the activity of tissue metabolism. Drastic purgation by hypertonic salt solutions and the encouragement of profuse sweating by Turkish baths have had, and still have, their vogue as treatments of obesity. Quite apart from the fact that long-continued use of these methods, especially the former, may be exceedingly deleterious to the general health, their effects—though considerable at the time—are transient and short-lived, being almost entirely due to a temporary loss of water from the body. The two most practical procedures, therefore, are the use of rationally constructed subcaloric diets and occasionally the administration of a metabolic stimulant such as thyroid.

### DIETETICS

**Calories.**—In constructing a diet for obesity, certain physiological principles must be taken into account. The most important consideration is the total calorific value of the diet. In really obese people the total calories should not exceed 25 calories per kilogram of the standard body-weight, which represents the requirement of the healthy individual under basal conditions. In practical therapeutics it is quite superfluous to enter into such elaborately meticulous dietetic refinements. None the less, some consideration should be paid to the height, age and nutrition of the patient concerned. For ordinary purposes the prescription of a diet of 1,000 or

# AVERAGE WEIGHTS FOR WOMEN OF DIFFERENT HEIGHT AND AGE

15 to 55 years of age with indoor clothes and shoes. 6 lb. are allowed for clothes and 1½ in. for shoes.

Height in feet and inches. Weight in stones and pounds.

Height.	AGE.													
	15.	17.	19.	21.	23.	25.	28.	31.	34.	37.	40.	43.	46.	50.
Ft. In.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.
4 8	7 3	7 5	7 7	7 9	7 10	7 11	7 13	8 1	8 3	8 5	8 7	8 9	8 11	8 13
4 9	7 5	7 7	7 9	7 11	7 12	7 13	8 1	8 3	8 5	8 6	8 9	8 11	8 13	9 1
4 10	7 7	7 9	7 11	7 13	8 0	8 1	8 3	8 5	8 7	8 8	8 11	8 13	9 1	9 3
4 11	7 8	7 11	7 13	8 1	8 2	8 3	8 5	8 7	8 9	8 10	8 13	9 1	9 3	9 5
5 0	7 9	7 13	8 1	8 3	8 4	8 5	8 7	8 9	8 11	8 12	9 1	9 3	9 5	9 7
5 1	7 11	8 1	8 3	8 5	8 6	8 7	8 9	8 11	8 13	9 0	9 3	9 5	9 7	9 9
5 2	8 0	8 4	8 6	8 6	8 9	8 9	8 11	8 13	9 1	9 3	9 6	9 8	9 10	9 12
5 3	8 3	8 7	8 9	8 11	8 12	8 12	9 0	9 2	9 4	9 6	9 9	9 11	9 13	10 1
5 4	8 6	8 10	8 12	9 0	9 1	9 2	9 4	9 6	9 8	9 10	9 12	10 0	10 1	10 4
5 5	8 8	8 13	9 1	9 3	9 4	9 5	9 7	9 9	9 12	10 0	10 2	10 4	10 6	10 8
5 6	9 0	9 3	9 5	9 7	9 8	9 9	9 11	9 13	10 2	10 4	10 6	10 8	10 10	10 12
5 7	9 4	9 7	9 7	9 11	9 12	9 13	10 1	10 3	10 6	10 8	10 10	10 12	11 0	11 2
5 8	9 8	9 11	9 13	10 1	10 2	10 3	10 5	10 7	10 10	10 12	11 0	11 2	11 4	11 7
5 9	9 12	10 0	10 2	10 4	10 6	10 7	10 9	10 11	11 0	11 2	11 4	11 6	11 8	11 11
5 10	10 2	10 4	10 6	10 8	10 10	10 11	10 13	11 0	11 3	11 5	11 7	11 9	11 11	12 1
5 11	10 7	10 9	10 11	10 12	10 13	11 0	11 2	11 3	11 6	11 8	11 10	11 12	12 1	12 5
6 0	10 12	11 0	11 1	11 2	11 3	11 4	11 6	11 7	11 9	11 11	11 13	12 2	12 4	12 8

# AVERAGE WEIGHTS FOR MEN OF DIFFERENT HEIGHT AND AGE

15 to 55 years of age with indoor clothes and shoes. 10 lb. are allowed for clothes and 1 in. for shoes.

Height in feet and inches. Weight in stones and pounds.

Height.	AGE.													
	15.	17.	19.	21.	23.	25.	28.	31.	34.	37.	40.	43.	46.	50.
Ft. In.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.	St. Lb.
5 0	7 9	7 13	8 3	8 6	8 8	8 10	8 13	9 1	9 2	9 3	9 5	9 6	9 8	9 8
5 1	7 11	8 1	8 5	8 8	8 10	8 12	9 1	9 3	9 4	9 5	9 7	9 8	9 10	9 10
5 2	8 0	8 4	8 8	8 11	8 13	9 0	9 3	9 5	9 6	9 7	9 9	9 10	9 12	9 12
5 3	8 3	8 7	8 11	9 0	9 2	9 3	9 6	9 8	9 9	9 10	9 12	9 13	10 1	10 1
5 4	8 6	8 10	9 0	9 4	9 6	9 7	9 9	9 11	9 12	10 0	10 1	10 2	10 4	10 4
5 5	8 10	9 0	9 4	9 8	9 10	9 11	9 13	10 1	10 2	10 4	10 5	10 6	10 8	10 8
5 6	9 0	9 4	9 8	9 12	10 0	10 1	10 3	10 5	10 6	10 8	10 9	10 10	10 12	10 12
5 7	9 4	9 8	9 12	10 1	10 3	10 5	10 7	10 9	10 10	10 12	10 13	11 0	11 2	11 2
5 8	9 8	9 12	10 2	10 5	10 7	10 9	10 11	10 13	11 1	11 3	11 4	11 5	11 7	11 7
5 9	9 12	10 2	10 6	10 9	10 11	10 13	11 1	11 3	11 6	11 8	11 9	11 10	11 12	11 12
5 10	10 2	10 6	10 10	10 13	11 1	11 3	11 5	11 8	11 11	11 13	12 0	12 1	12 3	12 3
5 11	10 7	10 11	11 1	11 0	11 5	11 8	11 10	11 13	12 2	12 4	12 6	12 7	12 9	12 9
6 0	10 12	11 2	11 6	11 8	11 10	11 13	12 2	12 5	12 8	12 10	12 12	12 13	13 1	13 1
6 1	11 3	11 7	11 11	11 13	12 1	12 5	12 8	12 11	13 0	13 2	13 4	13 5	13 7	13 8
6 2	11 8	11 12	12 2	12 4	12 7	12 11	13 0	13 3	13 6	13 9	13 11	13 12	14 0	14 1
6 3	11 13	12 3	12 7	12 9	12 12	13 2	13 6	13 9	13 12	14 1	14 4	14 5	14 7	14 8
6 4	12 4	12 8	12 12	13 0	13 3	13 7	13 11	14 1	14 4	14 7	14 10	14 12	15 0	15 1

1,200 calories is all that is necessary. Occasionally, a hard-working man may require one of 1,500 calories, but it must be remembered that unless the patients are under close supervision in hospital, it is safe to assume that they will tend to be liberal in interpreting their diets. Thus diets of 1,500 calories or over are usually singularly unsuccessful in reducing the weight of an out-patient, though they may well do so in hospital. On the other hand, diets with a value of less than 1,000 calories are unsuitable for patients who are not confined to bed. They are seldom adhered to, and if they are observed in the letter they cause weakness, faintness and an unduly rapid loss in weight. An 800 calorie diet may be employed, however, in resistant cases under observation in hospital.

**Fat.**—Consideration has not only to be given to the total number of calories provided, but also to the proportion of the basic foodstuffs (carbohydrate, protein and fat). In deciding the quantity of fat to be allowed it is assumed that, as the body will call upon its own stores, this substance can be reduced to a minimum in the diet. Some régimes allow no added fats, the patients merely getting the fat which is inseparable from other foods (such as meat) and, in consequence, the daily intake of fat may be as low as 20 gm. To compensate for its absence, fat-soluble vitamins in specially concentrated preparations have to be added. This *extreme* reduction of fat makes the diet difficult and unpalatable and is, moreover, unnecessary, since the content of fat in a diet does not seem to affect weight reduction to the same extent as its content of carbohydrate provided the total calories are kept unchanged. The diets given below contain from 40 to 50 gm. of fat.

**Carbohydrate.**—Since excess carbohydrate eating is the most important single ætiological factor in obesity, the carbohydrate should be restricted as far as possible in obesity diets. Sufficient carbohydrate, however, must be given to avoid the feeling of weakness and faintness which severe curtailment of carbohydrate intake so frequently occasions, and to avoid the occurrence of ketosis with its concomitant headaches. In addition, carbohydrates are the most powerful spacers of protein and their too severe restriction leads to excessive loss of body nitrogen. These effects can be avoided by giving not less than 100 or more than 130 gm. of carbohydrate a day. The greater part of the carbohydrate should consist of fruit and green vegetables. These give bulk to the diet and a considerable quantity of such foods can be taken without causing much addition to the patient's calorific intake. This has the double effect of causing a feeling of satiety and at the same time of providing the roughage to combat constipation, which subcaloric diets always tend to produce.

**Protein.**—Because of its stimulating action on metabolism, protein was often given in large quantities in reducing diets (*e.g.*, Banting and Salisbury diets), but as this means a higher calorific intake its advantage is somewhat doubtful and such diets are ill-balanced, expensive and impracticable in time of war. If, on the other hand, the protein of the diet is too low, a negative nitrogen balance will result from excessive destruction of tissue protein. The optimum intake of protein for a subcaloric diet should vary from 60 to 80 gm. per day.

**Salt.**—Apart from alcohol and sweetened drinks, no attempt need be made to restrict fluids, but the intake of sodium chloride should be curtailed. Salty foods should be avoided and as little table salt as possible should be taken.

## OBESITY DIETS

*Notes.*—The following notes apply to all the sample obesity diets given:—

The helpings of food are expressed in ounces instead of in grammes, since a reducing diet is most often used in the patient's home. If weighing on gramme scales, 1 oz. may be reckoned as 30 gm.

Bread and butter should be weighed and milk must be measured. It is convenient to measure the butter and milk in the morning and use them as desired throughout the day.

No foods are "slimming" foods.

Toast is no less fattening than bread.

Salt is to be taken in moderation.

*Foods to be Avoided.*

Sugar, sweets, jam, etc.

Scones, cakes, pastry, cereals.

Thick soups and sauces made with flour or butter.

Fried foods, cream and salad dressings.

Pork, duck, goose, fat meat and bacon.

Sweet wines, beer, stout, spirits or sweet aerated waters.

Nuts.

*Fruits—*

Dried, canned in syrup, bananas.

Grapes and plums allowed in moderation only.

*Vegetables—*

Potato, dried or fresh peas, dried beans, parsnips.

Beetroot allowed in small quantities only.

*Foods with no appreciable Caloric Value.*

Oxo, bovril, marmite, clear soups. (Avoid excess of meat extracts because of their salt content.)

A dessertspoonful of sugarless marmalade or jam (as sold for diabetics).

Gelatin, egg-white, green vegetables, vinegar, tea, coffee, unsweetened pickles.

Mineral oil, *i.e.*, liquid paraffin, can be used in place of fat for frying or instead of olive oil to make mayonnaise dressing.

## NO. 1. INEXPENSIVE OBESITY DIET

Carbohydrate, 100 gm.

Protein, 60 gm. (approximate daily average).

Fat, 40 gm. (approximate daily average).

Calories, 1,000.

*Breakfast—*

\*Orange or  $\frac{1}{2}$  grapefruit without sugar.

Bread, 1 oz. (1 thin slice); or 2 pieces of ryvita or vita-weat.

Butter from ration.

1 egg, or 1 oz. lean cold boiled ham or tongue or grilled sausage, or average helping of finnan haddock.

Tea or coffee with milk from ration.

\* If unavailable, fruit can be replaced by  $\frac{1}{2}$  oz. of extra bread or two water biscuits, which give approximately the same number of calories.

*Dinner—*

Clear soup, or marmite, or oxa, or bovril, if desired.

A medium helping (2 to 3 oz.) of cooked *lean* meat, chicken, rabbit, tripe or white fish. (If fish is taken,  $\frac{1}{4}$  oz. butter may be used for cooking.)

A large helping of vegetables, preferably from Group I (see p. 350). (See list of those to be avoided.)

\*1 apple, or pear, or other fruit (except those forbidden).

*Tea—*

(Now or at supper)—1 egg, or  $\frac{3}{4}$  oz. cheese, or medium helping of white fish, lean meat, chicken, or 1 oz. cooked lean ham or tongue.

Fresh salad or tomato.

Butter from ration.

Bread, 1 oz.

Tea or coffee with milk from ration.

*Supper—*

Bread, 1 oz.; or 2 pieces of ryvita or vita-weat, or 3 water biscuits.

Butter from ration.

Skim milk from ration; coffee, if desired.

\*1 medium-sized orange, or choice from the list.

*Rations for Day—*

Butter,  $\frac{3}{4}$  oz. | Skim milk,  $\frac{1}{2}$  pint.

No sugar. Saccharin or saxin can be used.

Water, 4 glasses, preferably not with meals.

To increase this diet to 1,100 calories give whole milk in place of skim milk.

To increase further to 1,200 calories add  $\frac{1}{2}$  oz. butter.

## No. 2. OBESITY DIET

Carbohydrate, 116 gm.

Protein, 70 gm. (approximate daily average).

Fat, 52 gm. (approximate daily average).

Calories, 1,200.

*Breakfast—*

\*1 orange or  $\frac{1}{2}$  grapefruit—saccharin may be used, but no sugar.

Tea or coffee with milk from ration.

1 egg, or 1 oz. cold lean ham or tongue or grilled sausage, or average helping finnan haddock.

1 oz. bread (1 thin slice). | 1 small pat of butter,  $\frac{1}{4}$  oz.

*Dinner—*

Clear soup, if desired.

An average helping of lean meat, poultry or game (2 to 3 oz.), or white fish.

No goose, pork or duck.

A large helping of any vegetable, except potato, dried peas, beans or lentils.

Fresh salad when possible (no oil or cream in dressing).

$\frac{3}{4}$  oz. cheese.

$\frac{1}{2}$  oz. ( $\frac{1}{2}$  thin slice) brown bread, or 2 plain biscuits—no butter.

\*Fresh fruit, except bananas, grapes or plums.

Coffee with milk from ration.

No sweet wine, beer, stout, spirits or sweet aerated waters.

\* If unavailable, fruit can be replaced by  $\frac{1}{2}$  oz. of extra bread or two water biscuits, which give approximately the same number of calories.

*Tea—*

Tea with milk from ration—saccharin instead of sugar, if wanted.

Bread,  $1\frac{1}{2}$  oz. ( $1\frac{1}{2}$  thin slices).

Tomato, lettuce or cress for a sandwich.

Small pat of butter,  $\frac{1}{4}$  oz.

*Supper—*

Clear soup, if wanted.

Fish, 3 oz. (cooked weight), *or* 1 egg, *or* 1 oz. boiled lean ham or tongue.

Vegetable or salad as at dinner. | \*Fruit as at dinner.

Milk from ration for curds, *or* with coffee, *or* make a custard, using the egg from breakfast.

Bread,  $\frac{1}{2}$  oz.; *or* 1 piece of ryvita.

*Rations for Day—*

Butter,  $\frac{3}{4}$  oz. | Milk,  $\frac{1}{2}$  pint.

Water, 4 glasses, preferably not with food.

No sugar.

If preferred, tea and supper can be interchanged.

To increase this diet to 1,500 calories:

	Cals. Approx.
Add Butter, $\frac{3}{4}$ oz. . . . .	171
Cheese, $\frac{3}{4}$ oz., <i>or</i> 1 egg . . . . .	78
Bread, $\frac{3}{4}$ oz. . . . .	56
Total extra cals. . . . .	<u>305</u>

In the case of women or young people extra milk is often preferred.

	Cals. Approx.
Milk, $\frac{1}{2}$ pint . . . . .	200
Butter, $\frac{1}{2}$ oz. . . . .	112
Total extra cals. . . . .	<u>312</u>

### NO. 3. EXPENSIVE OBESITY DIET

This diet allows for greater variety than Diets 1 and 2. It includes more expensive foods and has a higher protein content. Under conditions of rationing it will be found impracticable.

Carbohydrate, 100 gm.

Protein, 84 gm. (approximate daily average).

Fat, 52 gm. (approximate daily average).

Calories, 1,204.

*Breakfast—*

Tea or coffee with milk from ration.

Ryvita or vita-weat, 2 pieces; *or* bread (preferably brown), 1 oz. (1 thin slice).

Butter, 2 small balls ( $\frac{1}{2}$  oz.) from ration.

Fresh peach, slice of melon,  $\frac{1}{2}$  grapefruit or orange.

1 egg; *or* 1 oz. cold lean ham or tongue. (If preferred, use the egg for custard or serve as a savoury at dinner.)

\* If unavailable, fruit can be replaced by  $\frac{1}{2}$  oz. of extra bread or two water biscuits, which give approximately the same number of calories.

*Lunch—*

Tomato juice cocktail, if desired.

Meat: Medium-sized helping of cooked *lean* meat (2 to 3 oz.), or chicken, or game, or white fish—a good-sized fillet, grilled or baked with  $\frac{1}{4}$  oz. extra butter.

Or 2 eggs as omelette, with butter from ration. Mushroom or kidney can be added, also herbs and seasoning.

Or Aspic jelly with cold shell-fish, chicken, game, or egg.

Vegetable: Salad of lettuce, cucumber, tomato, radishes, asparagus tips, etc. Vegetable, as desired, except those forbidden (see list, p. 387).

Fruit, *e.g.*, apple or pear, etc. (see list to be avoided).

Cheese, one section,  $\frac{3}{4}$  oz.

Ryvita or vita-wheat, 2 pieces; or 3 water biscuits.

Coffee, if desired, with milk from ration.

*4 p.m.—*

Tea, if desired, with milk from ration.

*Dinner—*

Clear soup, if desired.

\*Fish: Fillet of sole (approximately  $2\frac{1}{2}$  oz.) grilled with butter from ration.

Or lobster or crayfish (mineral oil mayonnaise). Salad as desired.

Or 1 doz. oysters—lemon juice.

\*Meat: Noisettes of mutton (centre of 2 grilled cutlets=2 oz. meat).

Or chicken, game or braised sweetbread.

Vegetable, except those forbidden (see p. 387).

Fresh fruit as before.

Ryvita, 1 piece; or  $\frac{1}{2}$  slice thin toast.

Milk from ration can be used for curds, milk jelly custard (using egg from breakfast, or omitting fish); or sauce can be made with butter from allowance and 1 teaspoonful of flour (omitting ryvita, 1 piece). Flavour with vinegar, lemon juice, tomato purée, anchovy essence, parsley mushroom or a few oysters.

*Rations for Day—*

Milk,  $\frac{1}{2}$  pint. ; Butter,  $\frac{3}{4}$  oz.

No sugar. Saxin or saccharin, if desired.

To increase this diet add extra butter, which will greatly add to the palatability. Each  $\frac{1}{2}$  oz. butter=112 calories.

**Diet in Complications.**—Obesity is often associated with complications, and some modification of the above diets may be necessary.

*Constipation.*—If constipation is present larger helpings of green vegetables should be taken. Two tablespoonfuls of Kellogg's All-Bran can be given at breakfast (calories, approximately 100).

A dessertspoonful of shredded agar-agar, taken once or twice a day with meals, is useful but expensive.

Buttermilk is helpful, and the ration of sweet milk can be reduced. One pint of buttermilk gives 200 calories.

\* If both fish and meat are not desired, a large helping of either could be taken, *e.g.*, 2 fillets of fish or  $\frac{1}{4}$  lb. grilled fillet steak.

If fish only is taken,  $\frac{1}{4}$  oz. extra butter may be allowed for cooking.

*Cholecystitis*.—If the obesity is complicated by cholecystitis or gallstones, egg yolks should be omitted and extra fish or chicken substituted. Vegetables which may produce flatulence should be omitted, *e.g.*, cabbage, brussels sprouts, peas, turnip, onions. If necessary, other vegetables may be served in purée form. Hot water should be given before breakfast, at bedtime and between meals.

*Cardiac Diseases*.—Bulky diets are unsuitable in cardiac cases. Very little fluid should be given with meals. The vegetables should be sieved and only served with the midday meal, and supper should be light and taken early in the evening. If oedema is present salt should be drastically restricted.

*Hypertension*.—Low protein diets are sometimes prescribed for obesity with hypertension, but there is little evidence that restriction of protein reduces the blood pressure. There is no doubt, however, that a reduction in the patient's weight is an important factor in this respect. If the hypertension is associated with renal insufficiency of the azotæmic type the cooked protein may be omitted from the evening meal, especially in the higher protein diets. Unlimited amounts of tea, coffee and highly salted meat extracts are undesirable in hypertension.

### THYROID

The well-known stimulating effects of thyroid on the metabolism have been utilized in the treatment of obesity since the end of the nineteenth century. Its popularity has waxed and waned. Formerly large doses were given, but as its limits and dangers have become recognized, more conservative tendencies have prevailed. Many modern writers warn against its promiscuous use in obesity and some consider it irrational and dangerous, since it may cause a degree of hyperthyroidism resulting in an overstrained myocardium. This latter extreme view is far too narrow. The mere fact that a drug is dangerous when improperly used is not an argument for its banishment from the pharmacopœia. It is true that most obese patients can be treated quite satisfactorily by careful dieting, and for them thyroid is as unnecessary as insulin for the mild diabetic. It is also true that many obese persons with overstrained hearts are intolerant to thyroid, even in small doses, and rapidly develop tachycardia and palpitation under its influence. For them, also, the use of thyroid is contraindicated. In any case, the patient should never be given a prescription for thyroid and be allowed to continue to take the drug indefinitely without medical supervision. Serious permanent damage, especially to the myocardium and nervous system, may result from such methods. Patients taking thyroid should be seen regularly, and any evidence of undue tachycardia should be an indication for reducing the dose or for withdrawing the drug altogether. Sometimes its use seems to cause tremor, nervousness and, occasionally, diarrhoea, symptoms which again indicate an intolerance to the drug. While thyroid should, therefore, be prescribed with caution, it is undoubtedly of service when definite subthyroidism is present, or when the weight lost with a subcaloric diet alone is unsatisfactory. It is a useful drug if properly handled and, when definitely indicated, is invaluable.

If it were possible to be certain which endocrine gland was mostly at fault in certain cases of obesity, more specific hormones than thyroid might



be used. Endocrine preparations other than thyroid, however, have either no effect or very inconsistent effects on the obesity itself—whatever other beneficial results may accrue from their use. Further, few other endocrine preparations, apart from thyroid, are active when given by the mouth, and it is impracticable—or at least inconvenient—to treat obesity by frequent injections. Lastly, most other potent and properly standardized endocrine preparations are exceedingly expensive.

Unfortunately, thyroid is procurable in a large number of different forms, giving rise to an inconvenient and possibly dangerous confusion as regards dosage. It is, therefore, much better to confine oneself to the prescription of the standardized pharmacopœial preparation (thyroid, B.P.). Unstandardized thyroid preparations, whether of fresh gland or dried extract, may vary more than sixfold in their content of active material. The average dose of thyroid is 1 gr. (0.06 gm.) twice a day, which can be increased or decreased as found necessary, the pulse-rate being the chief guide to the size of the dose. As it takes at least a month for a daily dose of thyroid to produce its full effect, a considerable time should be allowed to elapse between each increase in dosage.

### OTHER DRUGS

Synthetic preparations of thyroxine are expensive and have no advantages over the pharmacopœial preparation. Other metabolic stimulants such as dinitrophenol, which had a transient and disastrous popularity, should never be used. Dinitrophenol has powerful toxic effects, especially on the liver, and is no substitute for thyroid in myxœdematous states. Amphetamine sulphate, on the other hand, is a valuable subsidiary weapon in the treatment of obesity. By depressing the appetite it abolishes the distressing sensations of hunger which are so troublesome to some patients on subcaloric diets and which may cause them to eat more than has been prescribed. In addition, amphetamine dissipates the languor and depression which may be complained of by patients eating restricted diets. The drug should be given in 5 mg. doses before breakfast and before the midday meal. It should not be given in the evening owing to its tendency to cause insomnia. Just as some patients are intolerant to the sympathomimetic effects of ephedrine, so they may be unable to tolerate amphetamine, even in the small doses suggested, without experiencing palpitation, tremor and nervousness.

### THE CONTROL OF TREATMENT

Patients undergoing reduction in weight should be seen frequently by the doctor, even if they are not taking thyroid. Their dietetic enthusiasm tends to wane unless they receive constant encouragement, and occasionally mild bullying. It is important to warn them against taking sweets and chocolates and sweet drinks between meals. Unless they are so warned, many patients take these oddments quite innocently, thinking that there is little or no food value in such things. Again, many patients become careless about their diet when they go on holiday, or may be unable to procure it accurately in hotels or lodgings. The labour of months may be undone in this way in a few weeks. We have known, for example, one patient who regained 7 lb. during the course of a week's holiday, and this is not an exceptional case.

Patients should be weighed weekly, and an average loss of between 2 and 3 lb. a week should be aimed at. If the weight loss is constantly more rapid than this the diet should be slightly increased. When the loss, on the other hand, does not average 2 lb. a week, the patient should be carefully questioned as regards her strict observance of the diet, as slackness in this respect is far the most common cause of failure to lose weight satisfactorily. Occasionally, however, it may be necessary in such cases to modify the diet still further from perhaps 1,200 to 1,000 calories, or to give thyroid.

The rate of weight loss from day to day varies considerably. Such fluctuations are of little importance, though they occasionally make it difficult to ascertain the real rate of loss over short periods, and make it unnecessary to weigh the patient more than once a week. Some of these fluctuations may depend on whether or not urine or faeces have been evacuated before weighing, but changes in water balance probably account for most of them. In addition to these daily variations a disturbance in weight loss often accompanies menstruation. For two or three days before the period weight loss usually ceases, and a slight gain may occur, to be followed about the middle of the period by an increased rate of loss.

The influence of a subcaloric diet usually falls into three stages. During an initial period of a few days there is a rapid fall in weight, sometimes as much as 5 or 6 lb., which is probably largely due to fluid loss. Then follows a steady but diminishing loss, and lastly there may occur a phase in which the weight falls very slowly or is even maintained at a new level. Several explanations may be offered for this decreasing rate of weight loss. In part it may depend on the altering relationship of food intake to the body needs, for as the weight falls the total caloric requirements also diminish, and the discrepancy or deficit between these and the food supplied constantly becomes less. To some extent the phenomenon is due to a reduction in the metabolic rate, which invariably occurs on low caloric diets, and which is shown in its greatest degree in the completely fasting individual. This slowing of metabolism is an unavoidable disadvantage when attempting to effect weight reduction by means of a subcaloric diet alone, and justifies the use of small doses of thyroid to counteract its effects. Except in obviously subthyroid patients, it is wise to withhold thyroid till this flattening of the curve of weight reduction becomes obvious. The patients should be warned that the drug is not to be looked upon in any way as a substitute for dietetic treatment, but simply as a subsidiary measure.

No attempt should be made to reduce a very fat woman to the "ideal" weight for her height and age, given on p. 385, nor should girls in search of a fashionable figure be allowed to reduce themselves to unduly exiguous proportions. The practitioner must use his common sense in these respects.

It may be said that with rare exceptions all patients who keep to the régime outlined above lose weight satisfactorily, though they vary considerably in the rate at which this is done. Thus, those who are initially grossly overweight lose on the average more rapidly than those in whom the initial excess weight is only moderate. It might be expected that those cases who show an obvious disturbance of endocrine function would not respond satisfactorily to simple dietetic treatment. This, however, is not usually so, since the majority of cases of endogenous obesity seem to lose weight satisfactorily with dietetic treatment alone, though endocrine treatment may be advisable for other reasons. Again, the response to

treatment is very comparable in those who have been a long time fat, and in those who have only been fat for a few years. Long-standing obesity is, therefore, no drawback to successful treatment.

Unfortunately, once the weight has been satisfactorily reduced, there is usually a tendency for corpulence to return when treatment is entirely discontinued. Usually a slightly modified normal diet is sufficient to counteract this tendency. The patients have learned dietetic discretion and are generally able to maintain their weight at the new low level by the exercise of a little care, so that very strict dieting is no longer necessary. In a few unfortunate people, however, the slightest relaxation in dietetic care is followed by a rapid gain in weight. This tendency is most marked among patients with some definite endocrine disturbance. It is also frequently evident in those who were originally grossly obese and who have lost weight rapidly under treatment. Indeed, the greater the original obesity and the greater the response to treatment, the greater must be the care in relaxing treatment.

In conclusion, it may be said that there are few therapeutic measures in medicine so certain to produce results as the prescription of a subcaloric diet to an obese patient, provided the prescribed diet is strictly observed. In addition, there are few purely medical measures so likely to restore health or to prevent disability as the controlled weight reduction of excessively obese persons. Like so many other forms of therapy, however, much harm can be done by excessive enthusiasm; by an attempt to produce in a few weeks a result which should only be attained in many months, or by trying to slim people of already normal proportions. It must also be remembered that there is no royal road, nor even a short-cut, along which an obese person may travel safely to an ideal weight; but only along the thorny path of dietetic restriction, assisted, perhaps, in the steepest places by the stimulating influences of a little thyroid.

D. M. DUNLOP.

A. BUCHAN.

## DEFICIENCY DISEASES

### INTRODUCTION

Deficiency disease may be defined as a morbid condition caused by the lack of a sufficiency of one or more factors present in a good mixed diet. Prophylaxis, therefore, consists in making certain that the food contains all the proximate principles, minerals and vitamins in sufficient amounts; here we are concerned specially with the vitamins. Naturally, the requirements will vary with age, rate of growth and special conditions, such as pregnancy. As a general rule, it may be stated that anything which raises the metabolism will also increase the demand for the vitamins, and in this connection infection, toxæmia and pregnancy must be specially noted. Accordingly, when any extra strain is put on the organism, care must be taken that the supply of vitamins is sufficient.

Much has been written about the prevalence of what has been called subclinical hypovitaminosis. There is no doubt that milder degrees of vitamin deficiency may and do pass unrecognized because of cursory clinical examination and lack of appreciation of their early manifestations. This is specially liable to occur in infancy and childhood, during periods of active

growth and also in the female during pregnancy and lactation. It is possible that mild degrees of hypovitaminosis may frequently be found when special technical measures are used for their recognition. It is doubtful, however, whether the results of many of these can be taken as evidence of vitamin deficiency, and most authorities are agreed that the incidence of hypovitaminosis, which cannot be recognized by a careful and competent clinical observer, has been much overrated. Furthermore, when a mild deficiency state exists it can easily be eliminated in the majority of cases by the provision of an adequate mixed diet without having resort to special vitamin preparations. Although a platitude, it seems necessary to keep on reiterating that proximate principles and calories are as essential as vitamins. With good food everything essential is supplied, whereas with attention devoted exclusively to vitamins there is more than a risk that energy-yielding and body-building materials may be insufficient. Several investigations have clearly shown that the administration of vitamin supplements to healthy individuals consuming the ordinary diet of this country does not produce any beneficial effect that can be demonstrated.

The optimal vitamin requirements at various age periods are given below, but for the prophylactic treatment of hypovitaminosis little need be done for the individual with a healthy digestive system except to provide a good mixed diet. Care, however, must be taken when for any reason there is some interference with the processes of digestion or absorption. Thus the problem of hypovitaminosis C (see p. 403) may easily arise in patients with gastric ulcer, or hypovitaminosis B (see p. 398) in subjects suffering from alcoholism. We may summarize the factors which favour the development of avitaminosis as follows:—(1) inadequate intake resulting from dietary restriction (self-imposed, economic or therapeutic), improper cooking or gastro-intestinal upset such as anorexia and vomiting; (2) defective absorption resulting from coeliac disease, sprue, gastro-colic fistula, malignant disease of the alimentary tract or the prolonged administration of drugs which destroy vitamins in the gut; (3) decreased utilization such as may occur in disease of the liver; (4) increased requirement due to pregnancy, lactation, long-continued infections and hyperthyroidism. In these and similar cases special measures are required in order to ensure an adequate provision of the various vitamins.

Recommended Daily Allowances for Vitamins (adapted from table approved by Food and Nutrition Board of the National Research Council, U.S.A.):—

	Vitamin A. I.U.	Aneurin. I.U.	Riboflavin. Mg.	Nicotinic Acid. Mg.	Ascorbic Acid. Mg.	Vitamin D. I.U.
Adult. .	5,000	666	3.0	20.0	75.0	..
Infancy .	1,500	130	0.6	4.0	30.0	800
Childhood:						
1-3 years.	2,000	200	0.9	6.0	35.0	800
10-12 years.	4,500	400	1.8	12.0	75.0	..
Adolescence	5,000	666	3.0	20.0	100.0	..
Pregnancy .	6,000	600	2.5	18.0	100.0	800
Lactation .	8,000	700	3.0	23.0	150.0	800

The therapeutics of any deficiency disease is based on a knowledge of three things: (a) the clinical picture of the disease in question; (b) the diet required to make good the deficiency; (c) the highly concentrated preparations which are available for the supply of large amounts of the missing factor.

Generally, the administration of the vitamin required is a matter of little difficulty since oral administration suffices to replenish the supplies of the missing factor. It may be stated that in most cases the treatment of the less severe degrees of deficiency disease requires only natural food products, including cod-liver oil, and that expensive concentrates and proprietary articles achieve no additional purpose. With the severer forms of deficiency disease, highly concentrated products do offer a more rapid and at times a much more effective line of therapy. Occasionally, indeed, it may be necessary because of a very severe deficiency to supply the factor at a rate which cannot be accomplished by the oral route. Parenteral administration may also be required when intestinal absorption is defective, as may occur in sprue or in alcoholic neuritis.

It is important to remember that in deficiency diseases the deficiency is frequently multiple. Accordingly, in addition to supplying the vitamin, the lack of which is apparent, it is necessary to provide food containing an abundance of all essential factors.

The table below indicates some foodstuffs which contain relatively large amounts of various vitamins.

Vitamin A (or its precursor).	Vitamin B.	Vitamin C.	Vitamin D.
Liver.	Liver.		
	Kidney.		
	Lean meat.		
	Bacon and ham.		Mackerel.
Herring, eel and sardine.			Herring.
Fish liver oils.			Fish liver oils.
Cheese.			Tinned salmon.
			Egg-yolk.
	Whole-meal bread.		
	Oatmeal.		
	Nuts.		
	Peas and beans.	Potatoes in large amounts.	
	Rice bran.	Hips and Haws.	
	Yeast.	Brussels sprouts.	
	Marmite.	Tomatoes.	
	Bemax.	Oranges.	
Tomatoes.		Lemons.	
Spinach.		Grapefruit.	
Carrots.		Watercress.	
		Asparagus tips.	
		Parsley.	
		Black currants.	

### VITAMIN A DEFICIENCY

The most important function of vitamin A is to promote the nutrition of epithelial surfaces, and the regeneration of visual purple in the retina, and possibly also to maintain the healthy function of the nerve cells. In its absence the epithelial cells tend to atrophy, become keratinized and desquamate. As a result, epithelial ducts become choked with the fragments of dead and dying cells which afford a nidus for the growth of micro-organisms, which cause a low-grade inflammatory reaction in the devitalized epithelial layer. All epithelial surfaces are liable to be involved, but one may mention particularly the cornea, skin and urinary tract. In a recent investigation Leitner and Moore found no support for the view that vitamin A deficiency was associated with the common varieties of skin disease, but suggest that in Darier's disease, pityriasis rubra pilaris and ichthyosis the administration of massive doses of vitamin A may be of service. It is probable that one of the first manifestations of hypovitaminosis A is defective vision in dim light (nyctalopia), which is associated most frequently with chronic liver disease and disorders of digestion and absorption. In the less severe types of deficiency the administration of vitamin A in adequate amounts rapidly leads to revitalization of the affected tissues, usually within two or three weeks.

The ingestion of an adequate diet is without doubt quite sufficient to prevent any deficiency of vitamin A. It should be remembered that its absorption is greatly facilitated by the simultaneous absorption of fat. Carotene, the precursor and source of much of the vitamin A in the diet, requires the presence of bile in the intestine for adequate absorption. Furthermore, liquid paraffin may reduce the utilization of the provitamin by carrying away relatively large amounts in the faeces. Consideration of special measures for supplying this factor only arises when the diet is deficient as a result of poverty or idiosyncrasy, when absorption from the intestine is defective as in coeliac disease, or when requirements are increased as is likely in the presence of infection, etc. Although there is little doubt that a severe deficiency of vitamin A, as of any essential food, lowers resistance to infection, it is doubtful whether even very large doses of the vitamin exert a curative effect. The minimal requirements of vitamin A for the human subject are unknown, but it may be stated that 5,000 international units is certainly an optimal figure for a healthy adult. This is contained in rather more than a teaspoonful of cod-liver oil. A child needs roughly double the adult requirement because of the demands resulting from active growth. In pregnant and lactating women the demand for vitamin A is also increased; for them a daily intake of 8,000 international units (contained in 2 teaspoonfuls of cod-liver oil) has been recommended.\* A good general diet, however, containing some of the following—egg, liver, carrot, spinach and tomato—is all that is generally necessary to meet these requirements. If for financial or other reasons an adequate diet cannot be obtained it is advisable to give cod-liver oil or oleum vitaminatum. When the patient is unable or unwilling to take cod-liver oil, a vitamin A concentrate must be prescribed, such as liquor vitamini A concentratus (B.P.), Avoleum (B.D.H.) or Prepalin (Glaxo).

The actual dose varies with the intensity of the deficiency. When the manifestations of hypovitaminosis are severe, as much as 600,000 inter-

national units should be given daily. For milder degrees of deficiency a dose of 3 minims (0.17 c.c.), 1 capsule of one of the above preparations, three times daily, generally suffices. Usually, however, there is an associated hypovitaminosis D, in which case liquor vitaminorum A et D concentratus (B.P.), capsules of Adexolin (Glaxo), Radiostoleum (B.D.H.) or halibut-liver oil (Crookes) are to be preferred. Each of these preparations contains both vitamins A and D; in mild degrees of deficiency they should be given in doses of 3 minims (0.17 c.c.) or one capsule thrice daily.

In addition to the administration of the necessary vitamins, appropriate local treatment, for the lesions in the eyes, skin and mucous membranes, must be given. Drops of cod-liver oil can be instilled into the conjunctiva every morning and evening and  $\frac{1}{4}$  per cent. atropine ointment every night. For the skin a simple preparation such as zinc ointment suffices, while for mucous membranes a non-irritant antiseptic lotion such as hydrogen peroxide or euflavine 1 : 1,000 may be used.

### VITAMIN B DEFICIENCY

The vitamin B complex contains at least nine separate factors each of which appears to play a part in metabolism. Their exact significance in human nutrition is in many cases unknown. Even as regards vitamin B<sub>1</sub> some doubt has arisen as to its relationship to the development of the beriberi syndrome. Accordingly, it is more important than ever when dealing with vitamin B deficiencies of any kind, to ensure that the diet should contain a rich supply of all the B vitamins. At present facts about pyridoxine, pantothenic acid and certain other members of the complex are not sufficiently definite in relation to human nutrition to make it advisable to deal with them here.

**Beri-Beri.**—Beri-beri is prevalent in those countries where the common dietary habits result in a marked deficiency in the intake of aneurin (vitamin B<sub>1</sub>). In its florid form, characterized by severe multiple neuritis or signs of cardiac failure, it is rare in this country. Within the past few years, however, clinical studies have suggested that minor degrees of hypovitaminosis B<sub>1</sub> may be not infrequent, even in regions where the diet of the population had previously been considered satisfactory. Especially is this the case when for any reason absorption in the alimentary tract is defective. Thus in chronic alcoholism the general opinion appears to be that vitamin B<sub>1</sub> deficiency plays a very important part in the causation of polyneuritis. In some of the other forms of polyneuritis also it is possible that an insufficiency of B<sub>1</sub> has at least an aggravating influence.

Vitamin B<sub>1</sub> can now be obtained in a chemically pure state from natural sources, such as yeast, and can also be prepared synthetically. In this country it is called aneurin, in the United States, thiamin.

The minimum daily requirement for the healthy adult is said to be 2 mg. of aneurin (666 international units). This is contained in about 2 oz. of bemax, 2 oz. of marmite or one tablet of any of the proprietary brands of vitamin B<sub>1</sub>. Infants and children require relatively more, as much as 400 units being considered necessary at ten years of age.

It is important, however, to remember that vitamin B<sub>1</sub> requirements in man are dependent on body-weight, carbohydrate content of the diet and general metabolism. A high intake of carbohydrate necessitates an extra

supply of the vitamin. In addition, the demand for vitamin B<sub>1</sub> may be increased up to fivefold during pregnancy and lactation. Indeed, anything which increases the metabolism, *e.g.*, infection or hyperthyroidism, by raising the need for B<sub>1</sub>, may precipitate an attack of acute B<sub>1</sub> deficiency. Accordingly, in areas where beri-beri is rife, the onset of pregnancy or the presence of infection, as well as the appearance of early symptoms, is a signal for increasing the administration of vitamin B<sub>1</sub>.

The onset of hypovitaminosis B<sub>1</sub> is insidious. Its manifestations are varied and include general muscular weakness, especially of the quadriceps muscles, loss of appetite, vague abdominal pain with constipation, neuralgic pains with tenderness of the calves, hyperæsthesia of the feet and odd sensations of tingling in the limbs. Later, there is frank peripheral neuritis with circulatory disturbance indicated by tachycardia, dyspnoea, hypotension and œdema. In severe deficiency states there may be papilloedema, retinal hæmorrhages and ophthalmoplegia. It is obvious that many of these symptoms may be found in association with conditions other than defective B<sub>1</sub> intake or utilization. They should not therefore be attributed to hypovitaminosis without a complete investigation of the patient's history and condition.

In this country, at any rate, there is little need to worry about the intake of vitamin B<sub>1</sub>, unless the dietetic history suggests that the patient has been living on a diet consisting largely of highly refined foodstuffs. It should be remembered, however, that vitamin B<sub>1</sub> is rapidly destroyed in an alkaline medium. Accordingly, it seems probable that in conditions where the gastric secretion of hydrochloric acid is defective (primary or secondary hypochlorhydria and achlorhydria) the administration of B<sub>1</sub> must be carefully supervised and on the first indication of hypovitaminosis parenteral therapy adopted. This is specially necessary when there is any history of alcoholism. Alcohol renders B<sub>1</sub> very susceptible to destruction in an alkaline medium and in addition lessens and even completely prevents its absorption by the intestinal mucosa. Furthermore, disease of the liver may prevent the utilization of B<sub>1</sub> after its absorption.

The vitamin is found in relatively high amounts in yeast, wheat germ, bran, peas and beans, liver and kidney. It is destroyed by prolonged heating, but enough is left in these foods after the ordinary cooking processes to supply the needs of the body. In rice-eating countries much has been done by changing the diet from one of highly polished rice to one in which the rice is boiled and dried prior to the removal of the pericarp. Another method which has been used with some success in India is the daily administration of a freshly prepared infusion of rice bran or of a commercial extract of rice, ryzamin B (B. W. & Co.), in doses of 20 gr. (1.2 gm.) thrice daily; in addition, attempts are made to insist on the use of unhulled rice with as much vegetables and fruit as can be afforded. The adoption of this procedure suffices not only to prevent the onset of beri-beri but even to effect a cure in the milder cases.

Special diets used for the treatment of gastric or duodenal ulcer, cœliac disease, sprue or obesity may produce a mild degree of hypovitaminosis. It is of great importance to make certain that the diet contains a sufficiency of B<sub>1</sub>, or, if this is impracticable for financial or medical reasons, to provide a concentrate of the vitamin. For this purpose 1 oz. of bemax, a stable preparation of wheat germ, or 1 teaspoonful of marmite can be given daily; yeast tablets may also be used, 2 being given three times daily before meals.



When there is reason to suspect defective intestinal absorption vitamin B<sub>1</sub> can be injected intramuscularly: 1 ampoule containing 2 mg. of synthetic vitamin B<sub>1</sub>, equivalent to 666 international units, is the usual daily dose, but more may be given if it is thought necessary.

When obvious clinical manifestations of vitamin B<sub>1</sub> deficiency are already present no time should be lost in commencing treatment since there is always the danger of circulatory failure. Rest in bed is essential, care being taken, if neuritis is present, that the weight of the bedclothes is removed from the patient's limbs by a cage. While too much work should not be imposed on the digestive tract, it is important so to arrange the diet that a large amount of vitamin B<sub>1</sub> is ingested with a minimum quantity of carbohydrate. The feeds, therefore, should be small and frequent, consisting largely of the foodstuffs rich in the vitamin (see Table, p. 396). Yeast tablets, 2 to 4 three times a day before food, or marmite, 1 to 2 teaspoonfuls three times a day, is a suitable method of giving large doses of B<sub>1</sub> when there is no evidence of defective absorption. These substances have the advantage that they contain all the factors present in the vitamin B complex. A more certain method of ensuring an adequate supply of the vitamin is the intramuscular or intravenous injection of "crystalline B<sub>1</sub>." This overcomes the possibility of defective absorption which is apparently not infrequent in cases of B<sub>1</sub> deficiency. Numerous preparations are available. Two to five milligrams of a crystalline preparation should be given daily for a fortnight by one of the parenteral routes. For this purpose there are available preparations of vitamin B<sub>1</sub> supplied in ampoules each of which contains 2 mg. of the crystalline substance. Thereafter, treatment can be continued by the oral administration of vitamin B<sub>1</sub> preparations in the quantities already mentioned (2 to 5 tablets). When large amounts of vitamin B<sub>1</sub> are to be given parenterally it is wise to use special strong solutions, each ampoule of which contains 10 mg. In very severe cases 50 or even 100 mg. intravenously may be required, followed by daily intramuscular injections of 20 mg. for two weeks. After a period of intensive therapy the oral route can be adopted, the same amounts of B<sub>1</sub> being used until the patient is free of symptoms.

Aneurin has been generally considered non-toxic even in amounts greatly exceeding the daily requirement. Within recent years undesirable side effects including two deaths have been reported following oral and parenteral administration of the vitamin in large doses. The reported signs of toxicity have included allergic phenomena, such as urticaria and asthma, and nervous manifestations such as tremor, sweating, tachycardia and herpes zoster. Whether or not these phenomena are anaphylactic in nature, it would seem wise to limit parenteral administration of aneurin to patients who are acutely ill or are likely to have defective intestinal absorption because of diarrhoea or other digestive upset. When an intravenous injection is necessary it should be given very slowly.

Great improvement and even complete recovery may take place within a few weeks of the commencement of B<sub>1</sub> therapy provided the polyneuritis is not severe.

If paralysis is present, wrist and foot drop must be treated with appropriate splinting to maintain the extremities in the correct positions. Massage should be withheld until pain or tenderness have already disappeared, when it can be gently commenced along with galvanism. As improvement pro-

gresses, active as well as passive movements must be undertaken. All forms of muscular exercise must be very carefully graduated, and, in view of the risk of cardiac failure, should be carried out by the patient in bed until a considerable degree of recovery is manifest. Improvement is slow, at times very slow. With the severer cases months are required before appreciable restoration of function is noted. Regeneration of the axon is said to take place at the rate of about 1 mm. per day : accordingly, it is necessary to persevere with treatment and not be disheartened if the degree of recovery is slow.

Circulatory failure is an urgent feature in some cases. If cardiac decompensation is present it should be dealt with (p. 631). Generally the response of patients with circulatory failure to B<sub>1</sub> therapy is fairly rapid. Within a few days the pulse-rate falls, the strength of the heart-beat is increased and a large output of urine occurs, so that within two weeks the patient may lose the bulk of his œdema.

It may take two months or longer before all the signs and symptoms of cardiac failure disappear. The longer the previous duration of the disease the more prolonged will be the convalescence, since the myocardium may be seriously weakened in long-standing cases. Of the other manifestations of vitamin B<sub>1</sub> deficiency constipation is frequently troublesome, but will usually respond to the specific treatment, assisted when necessary by one or other of the anthracene purgatives.

During convalescence attention must continually be paid to the diet, which should be rich in vitamin B<sub>1</sub> and poor in carbohydrate, and should contain a sufficiency of other essential factors.

**Pellagra.**—Pellagra is a disease associated with a deficiency of nicotinamide, one of the factors in the vitamin B complex. It is commonly found in patients suffering from some dietary defect generally attributable to poverty, disorder of the gastro-intestinal tract, or refusal to take certain articles of food. It should be remembered that nicotinamide is synthesized by certain bacteria in the intestinal tract from which it is absorbed into the blood stream. The supply of the vitamin to the individual may thus be in large part endogenous and so may be greatly reduced by disease or the action of foodstuffs and drugs in altering the bacterial flora of the gut. The diets of pellagrins are poor in the foodstuffs which are relatively rich in B complex; another characteristic is a deficiency of protein of high biological value. In this country pellagra occurs chiefly among insane persons but is also found among alcoholics, individuals with cirrhosis of the liver and gastritis, and patients who have had short-circuiting operations on the alimentary tract. Recent reports indicate that the oral administration of sulphaquandine, succinyl sulphathiazole, sulphadiazine or penicillin may be followed by the appearance of signs of nicotinamide deficiency. While dermatitis, dementia and diarrhoeal disease characterize the well-marked case, milder degrees may occur and are recognized by pigmentation, dryness and scaliness of the skin, œdema and increasing redness of the tongue, fissure at the angles of the mouth and signs of nervous disturbance such as ataxia, unequal pupils and neuritis. Cruickshank and others have described a syndrome in prisoners of war in the Far East in which the chief features were aching and stabbing pains in the feet, occasionally associated with hypertension and exaggerated tendon reflexes. This is believed to be due to a deficiency of nicotinamide and possibly also of riboflavin.

Prophylaxis consists in the supply of foods rich in pellagra-preventing vitamin, *i.e.*, milk, lean beef, liver, chicken, rabbit, salmon, green peas, spinach, tomatoes, turnip, greens and yeast. In areas of the U.S.A. where pellagra is endemic, home gardening and the distribution of powdered yeast have yielded good results.

The specific treatment for pellagra is now generally recognized to be nicotinic acid, a constituent of the vitamin B complex. The richest sources of this substance among the ordinary foodstuffs are liver, kidneys, eggs, milk and cheese. It has been isolated from yeast and liver and can be produced synthetically. The normal daily requirements are said to be about 10 mg. For therapeutic purposes several proprietary preparations are available containing 50 mg. per tablet. It may be given in a solution of normal saline in daily amounts of 50 mg. by the intravenous or intramuscular route, but it is rarely necessary to give the drug parenterally. When given intravenously the injection of more than 50 mg. causes some slight discomfort, such as sensations of heat and tingling with peripheral vaso-dilatation and a slight fall of blood pressure. The oral route of administration is to be preferred. It is worth remembering that the amide of nicotinic acid is equal to nicotinic acid in therapeutic potency and much less likely to produce peripheral vaso-dilatation. Frequent small doses, such as 50 mg. at four-hourly intervals, are most successful in maintaining an adequate concentration in blood and tissues. Within twenty-four hours of the commencement of treatment improvement is noted and the desire for food returns. Two days later a significant change for the better is seen in the mental condition, and shortly afterwards the fiery red lesions of the buccal mucosa and the erythematous patches of the skin commence to disappear together with the excess porphyrinuria characteristic of pellagra. Little change is noted in the chronic skin lesions and no alleviation of the peripheral neuritis which is so often present.

Of equal importance with nicotinic acid therapy is a well-balanced diet rich in protein and poor in carbohydrate and fat. Restriction of the latter is advisable in order to avoid the production or aggravation of the digestive disorder which is so frequently associated with pellagra. The caloric intake should be as high as possible. Furthermore, the diet must be presented in a form which is easily digested by the alimentary tract. Lastly, it is most important to make certain that the prescribed foodstuffs are taken, and for this purpose individual nursing is very often necessary. Broths made from liver, lean meat and beef juice and fresh vegetable soups have all yielded good results. Dried brewer's yeast, containing as it does vitamin B<sub>1</sub> and the whole B<sub>2</sub> complex, is of particular value. If milk is to be the chief source of the antipellagra factor it is best given in the form of buttermilk in amounts of not less than 2 pints per day. By ingesting the articles of food mentioned above the pellagrous patient will tend to correct not only his deficiency of nicotinic acid but also the deficiency of vitamin B<sub>1</sub>, riboflavin, protein, iron and liver factor which may coexist.

Dried powdered yeast in amounts of 1 to 7 oz. per day has been found valuable. Liver extracts in large doses parenterally, or folic acid (see p. 486), are necessary where a macrocytic anæmia coexists. Achlorhydria is very frequently present and hydrochloric acid should be given in doses of 1 drachm (3.6 c.c.) of the dilute acid (B.P.) three times a day if diarrhoea is troublesome.

Gillman and Gillman obtained very good results in infantile pellagra by

the administration of dried stomach (ventriculin P.D.Co. 5 grams by mouth twice daily for six days) and state that the addition of vitamin concentrates to the ventriculin significantly detracts from its effectiveness as a therapeutic agent.

One of the characteristics of the disease is dermatitis, which is chiefly apparent in regions of the body exposed to light and friction. Patients should therefore be protected from direct sunlight, and, where necessary, a soothing ointment such as unguentum zinci oxidi (B.P.) can be applied to the skin. For stomatitis, which is frequently present, a bland antiseptic paint such as glycerinum acidi borici (B.P.) can be used.

In view of the dramatic improvement which results from the administration of nicotinic acid and an adequate diet the symptomatic measures outlined above are now seldom necessary.

**Riboflavin Deficiency.**—Riboflavin, a constituent of the vitamin B<sub>2</sub> complex, is found in liver, milk, cheese, eggs, yeast and green vegetables. It is apparently essential for growth and the maintenance of health, forming an important function in the enzyme system regulating the oxidation of carbohydrate compounds and the supply of oxygen to the tissue cells. The adult requirement has been estimated at about 1 to 3 mg. daily of riboflavin (600 Sherman Bourquin units). Cheilosis, sores on the lips and fissures at the angles of the mouth, is an early manifestation of riboflavin deficiency in man. In a more advanced stage glossitis, dermatitis and vascularizing keratitis with dimness of vision make their appearance. This condition can be effectively treated by crystalline synthetic riboflavin in doses of 5 to 10 mg. three times daily given by the mouth.

It is always advisable in addition to give a preparation containing all the members of the B complex since it is probable that pyridoxine and pantothenic acid play an important part in the mobilization and utilization of riboflavin. Accordingly 1 oz. of dried yeast should be given daily in divided doses.

Some patients with cheilosis do not respond to intensive therapy, and it is fairly certain that the lesions frequently occur independently of vitamin deficiency. Among ætiological factors are badly fitting dentures, sensitivity to lipstick or chewing gum and chronic iron deficiency anæmia, often of a mild degree. In the latter case the condition often responds to the administration of iron after large doses of the vitamin B complex have failed to exert a therapeutic effect.

### VITAMIN C DEFICIENCY

Frank scurvy, which is due to an inadequate supply of vitamin C or ascorbic acid, is in this country a comparatively rare condition. It is occasionally met with in infants and young children, especially those fed on some of the dried milks without supplements of some vitamin-C-containing food. It is also to be found among subjects with chronic alcoholism and old people living in lodging-houses whose diet has been extremely poor. It is possible that mild degrees of hypovitaminosis C are more frequent than has hitherto been supposed, but it is unlikely that such conditions are as widespread as some authors have stated.

Prophylaxis and treatment consists in ensuring an ample supply of ascorbic acid. Among the common articles of diet containing large amounts

of vitamin C are citrous fruits, black currants and tomatoes. Potato juice (uncooked) and sprouted vegetables are also fairly rich in ascorbic acid, a moderate amount of which is present in fresh beef and liver broth. In contrast to what has hitherto been believed, cooking destroys relatively little of vitamin C, but a proportion of this essential factor passes into the liquid in which the food is cooked. Recent work has shown that cooked but not overcooked vegetables contain a considerable amount of the vitamin, but use should be made of the water in which they are prepared. Tinned fruits certainly retain their vitamin C potency. Pasteurization may, and often does, lead to a destruction of the ascorbic acid of milk. The vitamin C content, however, even of fresh milk is insufficient by itself to meet the requirements of infants or children, so that its destruction is of little import, since in all circumstances more has to be provided.

The best preventive measure is undoubtedly the provision of a good mixed diet, taking special care that there is a plentiful supply of fruit and vegetables. When these are available there is no necessity for the wholesale distribution of tablets of ascorbic acid. The daily requirement of the adult is probably amply supplied by 50 mg. of ascorbic acid, while the infant's needs are met by 30 mg., the average content of half an orange. Relatively higher amounts are required during periods of rapid growth or when infections are present. In pregnancy and during lactation vitamin C requirements are also increased, as is the case when much muscular exercise is being undertaken. There is no doubt that during febrile states there is a greater utilization or destruction of vitamin C. Accordingly, a larger intake is required, especially if the fever is continued for more than a few days. This has long been, and can still be, quite efficiently accomplished by the administration of large amounts of fresh fruit juices (orange and lemon drinks). During the course of a prolonged illness, especially when associated with some infective process, great care must be taken to provide a sufficiency of vitamin C in food. This is also necessary when for any reason a patient is on a restricted diet, such as occurs in the treatment of gastric ulcer and various forms of dyspepsia. In these cases it may be necessary to give vitamin C in the form of ascorbic acid itself, which is available as tablets, each containing 50 mg. ascorbic acid: 2 tablets per day usually suffice. The infant's requirements of vitamin C are also high and it is necessary to provide this factor for the breast-fed as well as the artificially-fed baby. Orange juice, or some similar vitamin-C-containing fluid, should, therefore, always be included in the infant's dietary. The *minimal* daily amounts recommended are 1 teaspoonful of sweetened orange juice in the first month of life, gradually increased to 4 teaspoonfuls by the end of the third month. Tomato juice in double these amounts is equally efficacious.

When the symptoms and signs of scurvy have already appeared it is essential to give large doses of vitamin C. Here special standardized preparations of ascorbic acid are preferable to fruits whose content of vitamin C is variable. Occasionally the writer has encountered cases where the scorbutic condition has proved refractory to treatment, possibly as a result of the poor quality of the oranges supplied. Furthermore, the use of a concentrated preparation of ascorbic acid enables much larger doses to be administered than could conveniently be done with fruit juice.

One hundred and fifty to two hundred and fifty milligrams of ascorbic acid (3 to 5 tablets) should be given daily. When the condition is very

severe, or when there is any reason to suspect imperfect intestinal absorption, a parenteral route of administration may be chosen. Generally, an intramuscular injection is given, but if the patient is very ill the intravenous route should be used. For parenteral injection a 2 c.c. ampoule of any of the preparations of ascorbic acid, containing 100 mg., may be given, and this may be repeated three times daily for two or three days. The special *forte* preparation containing 500 mg. in 1 ampoule may be necessary when there is an urgent demand for vitamin C in large amount.

In addition to the administration of vitamin C general hygienic measures are required. Careful nursing in the acute stage is of very great importance, special care being taken to handle the patient as little as possible. Indeed, owing to the possibility of myocardial weakness, movement in bed should be reduced to a minimum. Clothing should be so arranged that it can easily be removed and changed. The limbs, which are painful as a result of subperiosteal hæmorrhages, should be lightly wrapped in cotton-wool and the weight of the bedclothes avoided by a cage. If the arms are tender they may be bandaged to the chest. For the lower limbs light splinting may be used. Frequently there is diarrhoea, but this has not to be taken as a contraindication to the administration of either ascorbic acid or orange juice, which indeed usually cures an apparently severe gastro-enteritis. If necessary, a sedative antidiarrhoeal mixture (chalk-mixture or bismuth with or without opium) can be given. For the bleeding from the mouth, bowel or urinary tract no special treatment is required, since it rapidly ceases with the administration of vitamin C. If there is marked anæmia, a blood transfusion may be necessary (see p. 933). Frequently the gums and mouth are foetid with patches of ulceration: a simple antiseptic mouth-wash such as hydrogen peroxide should be used. If the ulceration is severe the affected parts may be painted with 1 per cent. gentian violet.

Within twenty-four hours of the administration of vitamin C the pains diminish greatly, movement becomes easier and the patient brighter. Bleeding from the mouth and bowel rapidly stops, as does the hæmaturia, the cessation of which is accompanied by an increased output of urine. Subperiosteal hæmorrhages generally persist for a considerable time. Shortly after the initiation of vitamin C therapy the X-ray reveals a rapid deposition of calcium in the hæmatoma. Repeated skiagrams, however, show that it may take months before conditions in and around the bone return to normal. Indeed, a permanent arthritis may result.

Once the stage of convalescence has been reached, the diet should be increased, steps being taken to make certain that it contains ample vitamin C. At the same time attention has to be given to the necessity for dealing with other deficiency conditions, among which anæmia may specially be mentioned. The anæmia of scurvy responds to vitamin C alone, but as iron stores may also be depleted it is wiser to give iron as well. In this connection it is worth remembering that in certain cases of microcytic anæmia, when the hæmoglobin ceases to rise with iron therapy, the use of vitamin C has resulted in a steady improvement, as judged both by clinical and hæmatological standards.

As in the case of most other new drugs, ascorbic acid has been recommended as a panacea for many widely different diseases. Apart from scurvy and the anæmia which accompanies it, the administration of ascorbic

acid has led to insignificant results. Accordingly the indiscriminate use of proprietary preparations of ascorbic acid is to be deprecated.

### VITAMIN D DEFICIENCY

It is important for everyone responsible for the care of infants and young children to remember that while florid rickets may have all but disappeared, mild degrees of the rachitic process are still frequently found in the first two years of life by careful clinical, radiological and biochemical examination. A recent investigation, in which the writer took part, revealed the fact that about 50 per cent. of the infants admitted to the wards of a large municipal hospital showed definite signs of rickets, although only 3 per cent. were diagnosed as such on admission. The significance of mild degrees of rickets in relation to the future health of the child is not clear, but it seems reasonable to avoid any possible effects by ensuring an adequate retention of calcium, especially during periods when growth of bone is very active.

The most important factors in the ætiology of rickets are lack of sufficient exposure to sunshine and a diet defective in vitamin D. Although breast milk is undoubtedly the best type of infant food, it does not necessarily contain enough vitamin D to prevent rickets. The action of vitamin D is to promote the retention of calcium and phosphorus, and this is particularly important if the supply of these minerals is defective. In infancy milk is the staple food, so that an inadequate intake of lime must rarely be a factor in the production of rickets, unless human milk of a poor quality or a very dilute cow's milk mixture is supplied. During childhood, however, there appears to be no doubt that a dietary deficiency in calcium may be quite marked.

It is obvious that the prophylaxis and treatment of rickets resolves itself into ensuring an ample supply of calcium and vitamin D. Phosphorus may be left to look after itself, since it is hard to conceive of any human diet likely to be deficient in this element if a diet adequate in calcium is being taken. Milk, cheese and other milk products are the only satisfactory sources of lime, but it must be remembered that, quite apart from its bone-forming substances, milk contains elements of high biological value capable of stimulating growth. With the promotion of growth produced by a good milk intake, the development of rickets may actually be favoured, unless vitamin D is given in sufficient amount.

Before discussing the measures to be adopted in the prevention and treatment of rickets, it is necessary to consider the various forms in which vitamin D may be supplied, *viz.*, cod-liver oil and other fish-liver oils, concentrated preparations of vitamin D, irradiated milk and other irradiated foodstuffs, and the irradiation of the skin of the patient.

**Cod-liver Oil** (*oleum vitaminatum*, B.P.).—This is probably the easiest and certainly the cheapest method of administering vitamin D. It has the additional advantages of containing vitamin A and is itself of high caloric value. The infant is well able to assimilate cod-liver oil without digestive disturbance unless there is an idiosyncrasy to fat such as occurs in fat dyspepsia and coeliac disease. In some districts there is a tradition that cod-liver oil is harmful during warm weather, but there is no evidence to substantiate this view. Up till the past few years a valid objection to

the use of cod-liver oil might have been that its content of vitamin D was not guaranteed. Nowadays, however, the British Pharmacopœia insists on a minimum content of 85 international units per c.c. of the oil. Good brands of oil usually contain 100 units per c.c. Another objection frequently raised was the rancid odour and the fishy taste of the oil. The rancid odour is no longer present in modern preparations. The objection to the taste is not instinctive but acquired, usually as a result of the parent's or nurse's stupidity. It need hardly be said that even if the mother or nurse has a profound abhorrence of the taste and smell this should not be revealed to the child. It is neither necessary nor advisable to add orange juice or any flavouring agent to the oil, since with repeated administration infants and young children rapidly begin to like the taste and look forward to the oil. Care must be taken that the oil is entirely swallowed. With the child this is not difficult, but during the administration of the oil to an infant the baby's mouth should be kept open by pressing the cheeks inwards with the thumb and forefinger of the left hand while the oil is slowly poured into the mouth from a spoon held in the right hand. The mouth must be kept open until the oil has been swallowed: otherwise some may be expelled. There are possibly a few young children with an idiosyncrasy to cod-liver oil, but the one real contraindication to its use is the presence of fat intolerance, especially coeliac disease.

For prophylactic purposes, then, cod-liver oil is quite adequate. It should be given in doses of 10 minims (0.6 c.c.) daily at two weeks, 30 minims (1.8 c.c.) at four weeks, 60 minims (3.6 c.c.) at six weeks, gradually increasing to 2 drachms (7.2 c.c.) at three months. Although many rachitic infants have been completely cured by the use of cod-liver oil alone it is probably wise in the treatment of active rickets to fortify the oil by the addition of some vitamin D concentrate.

There is no advantage in preferring a cod-liver oil emulsion or a cod-liver oil and malt mixture. If sensibly handled, the young child does not require to have the taste disguised, and the use of these preparations simply makes it necessary for the patient to swallow larger amounts of medicine. Cod-liver oil emulsion may contain only 25 per cent. of oil and cod-liver oil and malt only 10 per cent.

**Halibut-liver Oil** has yielded excellent results in the prophylaxis and treatment of rickets. It is available as *oleum hippoglossi* (B.P.) and in commercial halibut-liver oil fortified with vitamins A and D (see Appendix). Other fish-liver oils have also been used successfully in the treatment of rickets and some form the basis of vitamin D concentrates, but none have achieved the popularity of cod-liver oil.

**Vitamin D Concentrates.**—Numerous brands are available, all being prepared from calciferol (crystalline vitamin D). The chief advantage obtained from the use of one of these concentrates is the ability to administer large doses of vitamin D in relatively small bulk. This is highly desirable in the treatment of a patient with active rickets and in the prophylactic treatment of those children with fat dyspepsia or an idiosyncrasy to cod-liver oil. At one time it was said that the vitamin D contained in a natural product such as cod-liver oil was more potent than calciferol in the treatment of rickets in the human subject. More recent work has shown that this is not the case, and carefully conducted clinical studies indicate that calciferol and cod-liver oil are equipotent, unit for unit, both prophylactically and



therapeutically. An objection that has been put forward to the use of vitamin D concentrates is the danger of hypervitaminosis D. This will be discussed later: here it need only be said that if the administration is kept within the recommended dosage the risk of poisoning is infinitesimal.

For prophylactic purposes a daily intake of 1 to 2 minims (0.06 to 0.12 c.c.) of liquor vitamini D concentratus (B.P.), equivalent to 500 to 1,000 international units, is to be recommended provided an ample supply of milk is being given. The therapeutic dose should not be less than 4 minims (0.24 c.c.) of the liquor (2,000 units).

Various other preparations of vitamin D concentrate are available, such as radiostol or ostelin (see Appendix). For prophylaxis in infants 6 to 15 minims (0.36 to 0.9 c.c.) daily should be given, and for active treatment 15 to 20 minims (0.9 to 1.2 c.c.), which may be added to the milk. For older children radiostol pellets or ostelin tablets, two or three daily, can be used. In some cases the concentrate is made up with calcium, but these preparations do not present any advantage as the amount of lime given is relatively insignificant. If there is any reason to suspect a vitamin A deficiency in the diet it is advisable to choose a preparation containing this factor. For this purpose 10 minims (0.58 c.c.) of adexolin or 30 minims (1.7 c.c.) of radio-stoleum daily can be given to infants with manifest signs of rickets. Capsules or pellets can be used for older children. For a list of proprietary vitamin D preparations, see Appendix.

During the past few years massive therapy with vitamin D has been introduced. One large dose of 600,000 international units given by the mouth suffices to cure rickets with or without tetany just as quickly and efficiently as repeated small doses. This form of therapy is specially useful for out-patient treatment when there is uncertainty as to efficient supervision at home. Preparations are available for intramuscular administration of vitamin D, *e.g.*, concentrated radiostoleum, which contains 15,000 international units of vitamin D and 75,000 international units of vitamin A. The parenteral route is, however, rarely necessary and does not yield more rapid results.

Mention may here be made of the different forms of vitamin D. It has been stated that the vitamin obtained from animal sources,  $D_3$ , is a more effective remedy in human rickets than calciferol or  $D_2$ , which is derived from plants. From the clinical point of view, it may be stated categorically that there is no difference between  $D_2$  and  $D_3$ .

**Irradiated Milk.**—An increase in the antirachitic activity of milk may be obtained either by adding a vitamin D concentrate to the milk, feeding the cows on irradiated yeast or irradiating the milk. The last variety has been used successfully both in the prevention and cure of rickets. It has the advantage of supplying other factors of prime importance. Its disadvantages are the inconstancy of the vitamin D content, which varies with the efficiency of the irradiating plant and the care with which the irradiation is done. Its use is only practicable in cities where pasteurization and irradiation can be combined and carefully supervised. There is a risk of inefficient therapy since the antirachitic potency of the milk cannot be determined prior to its use, whereas cod-liver oil and vitamin D concentrates can be and are standardized before they are marketed.

**Heliotherapy.**—Huldschinsky established the efficiency of direct irradiation.

tion of the skin with ultra-violet rays. These rays lead to the formation of vitamin D in the skin.

Only radiations with wave-lengths of less than 310 Angström units have any antirachitic potency. Quite apart from the pall of smoke which overhangs industrial areas, the atmosphere itself absorbs a large proportion of these short-wave radiations. Accordingly the greater the thickness of the atmosphere through which the sun's rays have to pass, the fewer the ultra-violet radiations that reach the earth's surface. It has been shown that the angle of inclination of the sun must be greater than 35 degrees before any ultra-violet rays get through. Thus direct sunlight in the winter months has little or no antirachitic potency in northern countries. Fortunately "skyshine," which is composed of the sun's radiations that have been reflected and scattered, has considerable antirachitic power. In the winter months the ultra-violet radiations of skyshine may far exceed those of direct sunshine. It should be emphasized, however, that in order to obtain the full value of skyshine nothing must intervene between the skin of the patient and any portion of the sky. Thus an infant at an open window facing open country will at best receive but half of the available ultra-violet irradiations. In a city street only a small fraction of rays of skyshine will fall even on those out of doors. Hence to get full value of either direct sunshine or skyshine it is necessary to take the child to an open space such as a park.

Since ordinary window-glass absorbs ultra-violet rays and renders them ineffective, the use of special glass with the property of being permeable to these rays has been strongly recommended. The generalized use of this form of window, however, would entail very considerable expense without corresponding advantage, since the amount of ultra-violet irradiation even through an open window diminishes rapidly as one moves inwards. This special glass may be of use in large institutions where it is impossible to take the infants out every day, but is certainly not worth while where they can be exposed daily to sun or skyshine, because on the days when weather conditions prevent children being taken out very little ultra-violet light can get through the atmosphere.

The formation of vitamin D in the skin as a result of ultra-violet irradiation takes place only in the exposed areas. Fortunately the exposure of a comparatively small area can, if sufficiently prolonged, have a marked antirachitic action. The smaller the area and the less intense the irradiation the longer must be the duration of the exposure. If heliotherapy is to play a significant part in the supply of vitamin D the infant or child must be taken into the open air, preferably in a field or park, for as long as possible and in all weathers except fog, storm or heavy rain. The presence of snow on the ground increases by reflection the intensity of the ultra-violet irradiation. The antirachitic potency of sunshine cannot be measured by the intensity of "sun-burn." This fact is worth stressing in view of the tendency noticeable in recent years to a return to sun-bathing. Indeed, prolonged exposure to the sun's rays, unless carefully regulated, may be followed by exhaustion, quite apart from the destruction of the skin by burning.

In conclusion, it may be said that exposure to sunshine or skyshine is a valuable adjunct to the prophylaxis of rickets, but in this country other measures in addition are generally necessary.

*Artificial Ultra-violet Light Irradiation.*—The most important effect of

ultra-violet light irradiation is the production of vitamin D from the ergosterol contained in the deeper layers of the skin. In addition, actinotherapy may produce erythema within a few hours, the erythema varying in intensity from simple redness to blistering, according to the degree and duration of irradiation. A late reaction is the deposition of melanin pigment in the dermis. This acts as a protection against over-dosage, but it gives no indication as to the general therapeutic effect of the irradiation. It should be remembered that the skin may become sensitized to ultra-violet light with resulting dermatitis. The liability to sensitization is increased by the presence of hæmatoporphyrin such as occurs in hæmatoporphyrinuria, by febrile conditions and by the administration of certain drugs, especially the heavy metals such as gold. Irradiation of the skin has a definite bactericidal action on the surface, but the power of penetration is very limited, so that no effect is produced in the ducts of sweat glands or the deeper layers of the epidermis. It is doubtful whether the bactericidal power of the blood is significantly increased.

Two types of apparatus are available: (a) carbon-arc lamp and (b) mercury-vapour lamp. The first may be employed when it is desired to irradiate with light and heat rays as well as with the ultra-violet rays. A current of at least 25 amps. must be used. When the ultra-violet rays are specially required the mercury-vapour lamp should be chosen. The mercury lamp should be allowed to burn for a few seconds prior to the exposure of the patient in order that the irradiation should reach a constant intensity. After the lamp has been used for some time the deposit of mercury which settles on the burner causes a reduction of efficiency, necessitating the cleaning of the burner.

Irradiation should be carried out in a well-ventilated room which is warm but not overheated. The eyes of all in the room must be protected from exposure with suitable coloured glass spectacles. The patient should be kept at a distance of about  $3\frac{1}{2}$  ft. from the lamp. First one side of the body is exposed, then the other. If a single patient is to be treated he should be on a couch, but if several are to be irradiated at once they may sit on chairs in a circle round the lamp.

Dosage must be judged for each patient. Erythema must always be avoided. In view of the possibility of undue susceptibility a very short exposure of one minute or less should be used for the first irradiation. The length of exposure should be gradually increased in succeeding treatments, which should be given every second or third day.

The main indications for ultra-violet irradiation are: (1) rickets and other conditions when there is defective retention of calcium, especially when there is some form of fat intolerance such as coeliac disease; and (2) infective states of the skin such as furunculosis, sycosis and acne. It is also of use in the treatment of lupus and non-pulmonary tuberculosis. Enthusiasts have recommended this form of treatment for numerous other conditions, but it is doubtful whether in many cases it has more than a psychological effect.

**Prophylaxis.**—This consists in the supply of vitamin D by one of the above-mentioned methods together with the provision of a suitable diet containing an abundance of lime and the institution of a satisfactory general hygiene. Open air provides a stimulus to the general metabolism, so that the child should be taken out every day unless weather conditions render

this unwise. The diet will vary with the age of the individual, but as soon as possible it should contain eggs, dairy foods, vegetables and fruits, and for older children the supply of milk should not be stinted, being kept at a level of 2 pints per day or even higher. It may be mentioned that neither pasteurization nor boiling of milk has any deleterious effect on the vitamin D content. Carbohydrates should not be given in excess. The fact that cereals have a rachitogenic effect which can be abolished by irradiation has led to the advocacy of irradiated cereals. The use of these expensive foods is quite unnecessary, nor is it necessary to stop the consumption of untreated cereals, since any rachitogenic effect that they possess can be effectively overcome by the provision of adequate vitamin D. The actual amounts of vitamin D which should be specially supplied depends on the diet, the daily exposure of the infant to skyshine or sunshine, and, most important of all, the rate of growth. The more rapid the increase in weight the more ample must be the supply of vitamin D. In general, it may be stated that a daily intake of 800 international units suffices for the full-term infant, while the premature infant requires about double this amount. Indeed, in some cases of prematurity it may be impossible to prevent rickets owing to the very rapid rate of growth.

*Maternal Treatment.*—It seems undoubted that the supply of milk and vitamin D to the expectant and nursing mother increases the calcium content of the newborn infant and raises the quality of the breast milk both as regards its concentration of lime and its antirachitic potency. During pregnancy and lactation care should therefore be taken of the mother's diet and hygiene, because in this way the susceptibility of the infant to rickets may be considerably reduced. It is wise, for this reason and also because of the demands made on the expectant and nursing mother for the supply of lime, to give her a diet containing abundant milk and a generous amount of vitamin D. This will prevent osteoporosis and osteomalacia minor degrees of which are probably much more frequent than is suspected, and are particularly evident in some forms of dental hypoplasia and caries.

Since there is definite evidence that the rachitic process may commence in the first month of life, prophylactic treatment should be commenced within two weeks of the infant's birth and ought to be continued for at least the first three years of life and preferably till much later. It must be carried on throughout all the seasons. Although the maximum incidence of rickets is in late winter and spring, it may occur at any time when growth is taking place and when the child is not supplied with a sufficiency of vitamin D.

*Treatment of Patient with Active Rickets.*—The essence of the therapeutic attack on rickets is the provision of an ample supply of lime and vitamin D. This can be achieved by a diet rich in milk and milk products, and the administration of one or other of the preparations with a high content of vitamin D. At least 2,000 international units must be given daily, and for the premature infant 3,000 or more units may be necessary. Elementary phosphorus, whether as phosphorated oil or in other form, is of no value, since it has no effect on the rate of healing of the rachitic process: it may induce deposition of lime in the juxta-epiphyseal region of the bone, but it does not promote the calcification of proliferating cartilage. Nor is there any need for other drugs. It must be remembered, however, that the rachitic infant frequently suffers from other defects besides that of vitamin D, so that it

may be necessary to supply iron to cure an attendant anæmia or vitamin C for associated scurvy.

It should be emphasized that while dietetic measures may prevent rickets it is certainly not sufficient to cure this disorder. Overfeeding should be avoided. In the first place the infant with rickets is liable to be affected by alimentary disorders, and, secondly, a high caloric diet may act as a stimulus to the growth process, with the result that more lime is required and the rickets becomes more acute. Consequently, during the active phase of rickets, the diet, while rich in minerals, should contain a limited amount of carbohydrates and cereals.

The bones, owing to their low content of lime, tend to be easily deformed. Accordingly as little strain as possible should be put on the skeletal system. The infant should be kept in bed and handled as little as possible, but he should not be allowed to lie for too long in one position in case curvature of the spine or other deformity should result. The older child should be kept off his feet and discouraged from using his upper limbs until the acute stage is passed. Once treatment has been initiated gentle massage and passive movements may be started, but it is generally found that as the rachitic process is cured the natural activity of the child increases and voluntary movements soon restore the natural tone to the muscles. Special medicated baths are quite unnecessary, although the stimulus of the ordinary bath is as valuable for the rachitic as for the healthy infant. Commencing deformities are often reduced by exercises specially adapted for each case. Particular care has to be taken, especially in the case of infants with deformities of the thorax, to prevent upper respiratory infections, which are liable to progress to a severe broncho-pneumonia.

One of the commonest accompaniments of rickets is tetany, which is specially liable to occur in the very early stages of healing, particularly if inadequate doses of vitamin D are being given. The treatment of this condition is dealt with elsewhere, but here it is worth stating that if there is any reason to suspect a tendency to spasmophilia extra calcium should be given in the form of gluconate or other easily assimilable salt (see p. 412).

**Results of Treatment.**—The rachitic patient begins to react to vitamin D administration within one week. By that time an increased retention of calcium and phosphorus can be demonstrated. Signs of healing cannot, however, be seen on the X-ray picture for two to three weeks, and about the same time is required before any alteration in blood chemistry (increase of serum inorganic phosphate and reduction of plasma phosphatase) is noted. Clinical improvement is rapid—the child becomes less irritable and fractious, ceases to perspire so profusely and is handled more easily. Soon an improvement in muscle tone is observed and the patient becomes more active. Cranio-tabes disappears quickly, but many of the bony deformities may be permanent. For some of the latter, such as contracted pelvis, nothing can be done, but considerable improvement of the less severe of the limb deformities may be achieved by orthopædic measures once the rachitic state has been completely healed.

**Hypervitaminosis D.**—Ever since it has been shown that massive doses of irradiated ergosterol could produce toxic symptoms of pathological changes in animals, reports have appeared of symptoms of overdosage in the human subject. There seems to be no doubt that some infants and children show an idiosyncrasy to vitamin D preparations—in one case even

a single drop of a concentrate was sufficient to produce violent vomiting. In such patients recovery from these symptoms is rapid after the administration of the vitamin is stopped. More serious is the statement that administration of vitamin D in high doses produces calcinosis affecting specially the kidneys.

Renal calcinosis was described by pathologists long before vitamin D was discovered and will continue to occur for reasons quite unconnected with this vitamin. Records are available of the administration of massive doses of calciferol for several weeks without any indications of toxicity. Recently, however, Debré and his colleagues have reported serious symptoms of calciferol overdosage in children. Anorexia, nausea, vomiting, signs of renal impairment and at times a clinical picture suggesting meningitis or a cerebral vascular catastrophe have been described. The serum calcium is usually high, as are the serum inorganic phosphate and blood urea, while X-rays may show evidence of calcification in the soft tissues and rarefaction of bones. In these patients the quantity of calciferol ingested varied from 60 to 150 mg. (2.4 to 6.0 million units) over a short period, amounts much in excess of those used for massive therapy in rickets. It may, therefore, be confidently asserted that vitamin D in the usual therapeutic doses is not fraught with any ill effect apart from the digestive disturbances that may occur in individuals with an idiosyncrasy to it. It would appear that toxic manifestations are particularly liable to occur in patients with constipation, diarrhoea or other gastro-intestinal upset. The threshold of toxicity for the human subject is said to be 20,000 units per kilo, but since toxic effects have been reported with an intake of 1,000 units per kilo a day it is wise to observe the patient closely if this dosage is exceeded, especially if very large doses are to be used, as is suggested for the treatment of lupus. Excessive increase in the values for serum calcium, serum phosphorus and blood urea and evidence of commencing renal impairment are indications that administration of the drug should be temporarily suspended, and the dose reduced if subsequent calciferol therapy is given.

*Refractoriness to Treatment.*—The presence of infection prevents the usual reaction to antirachitic therapy. Frequently recurring mild infections have a greater inhibitory effect than single acute attacks. Catarrh of the upper respiratory passages is particularly prone to favour the development of rickets and prevent its cure, possibly because the young patients are so frequently confined indoors. Every effort, therefore, should be made to keep these patients in the open air as much as possible, a procedure which will be of benefit in the management of the respiratory infection as well as for the prevention and treatment of rickets. Occasionally, even in the absence of infection, the rachitic state does not yield to treatment with the usual amounts of vitamin D. Increase in the dosage will generally overcome this refractory state unless there is some underlying constitutional abnormality.

**Celiac Rickets.**—Essentially there is no difference between celiac and ordinary infantile rickets. The important point to remember is that rickets is specially prone to occur when the growth impulse becomes active during a period of remission of the celiac disease. Care must be taken in treatment that calcium and vitamin D are supplied in forms that are likely to be utilized. For calcium, useful forms of administration are skimmed milk or dried milk with a low percentage of fat; these are available in the form of

Cow & Gate separated milk food (white label), prolac or buttermilk powder (G.L.). Vitamin D should be given with a minimum amount of oily substance. For this purpose concentrates in the form of tablets are particularly suitable, but it is here that ultra-violet irradiation finds one of its most beneficial applications.

**Renal Rickets.**—The pathogenesis of this condition has not been elucidated, but the rickets is merely a secondary feature of some profound underlying disturbance. Treatment, which at best can be merely palliative, is rendered extremely difficult by the fact that the mechanism regulating acid-base equilibrium is greatly impaired. Where renal inefficiency is marked the metabolism rapidly swings from acidosis, with its attendant uræmia, to alkalosis and tetany and vice versa. Although the administration of large amounts of vitamin D leads to an increase in the retention of lime it appears to do little to alter the course of the disease. Recently it has been shown that the use of an alkaline diet supplemented by alkalis and the addition of lime salts, such as calcium gluconate, may improve the renal condition. It may therefore be of advantage to give vitamin D with the object of increasing the retention of lime. The outlook in these cases is so gloomy that such a form of therapy is well worth trying, although it has been pointed out that the administration of vitamin D with a diet rich in calcium may lead to metastatic calcification.

**Osteomalacia.**—This disease may be defined as rickets occurring after osseous growth has been completed. It is therefore the result of vitamin D and calcium deficiency. The belief is still widespread that the ovarian secretions play a mysterious but important part in its pathogenesis. This is probably due to the fact that exacerbations are caused by pregnancy and lactation. This is not surprising when one remembers that the foetus makes a great demand on the calcium stores of the mother in the later months of intra-uterine life. It is necessary to emphasize these points in order to stress the fact that therapy is identical with that advised for ordinary infantile rickets. The diet must be ample and care must specially be taken to ensure an adequate supply of lime—in other words, milk, cheese and other milk products. Vitamin D must be supplied either as cod-liver oil or calciferol or by means of ultra-violet irradiation.

At least 4 pints of milk or its equivalent must be present in the daily diet. Should there be a scarcity of milk foods calcium can be given in the form of 2 drachms (7.8 gm.) of calcium lactate or gluconate thrice daily. Cod-liver oil, in amounts of 2 oz. per day, generally relieves the pains of the osteomalacic patient, but it is preferable to fortify the calcifying action of the oil by the addition of calciferol. Thus ostelin or radiostol can be given in doses of 30 minims (1.7 c.c.) daily. As in rickets, phosphorated oil has no value. Steps should also be taken to make good other deficiencies in the diet.

If labour has to be conducted in an osteomalacic patient, it is probably best to advise Cæsarean section. A repetition of pregnancy is very inadvisable until the osteomalacic condition is cured. Oophorectomy, although still holding a place of honour in a few textbooks, is no longer necessary; it probably received its place in the treatment of osteomalacia merely because of its action in preventing pregnancy. If calcium metabolism is restored to normal by an adequate dietary and vitamin D there is no reason why the patient should lose the benefit of the ovarian secretions.

**Osteoporosis.**—There is no doubt that in some cases, especially in the

elderly, this condition, which may be associated with fractures and deformities, may in part be due to defective intake of vitamin D and calcium. Care should be taken to ensure an adequate diet. Once the condition has become manifest the administration of vitamin D and calcium must be instituted, but unfortunately the response to treatment is often disappointing.

### TETANY

An appreciation of the pathogenesis of tetany is of great advantage when one is faced with the choice of suitable therapeutic measures. Clinical varieties of tetany are conveniently divided into two groups according as the serum calcium is or is not reduced. In the first, or hypocalcæmic group, are included cases associated with rickets, steatorrhœa, hypoparathyroidism and renal dysfunction; in the latter, or eucalcæmic group, are tetanies due to gastric disorder, bicarbonate administration and hyperventilation. While it is not conclusively proved, it is helpful from the therapeutic point of view to accept the hypothesis that the cause of the increased neuromuscular excitability is a reduction in the amount of ionized calcium. In hypocalcæmic tetany this fraction is diminished because of the fall in total calcium, while in the eucalcæmic group the ionized calcium is below normal limits as a result of an increase in the alkaline reaction of the blood.

The level of serum calcium can be raised in one of four ways: (1) by the parenteral administration of calcium; (2) by the administration of vitamin D together with a diet rich in lime; (3) by the injection of parathyroid extract; (4) by the administration of an acid-producing salt. Parenteral administration of calcium, especially if accomplished by the intravenous route, provides the most rapid method of raising the serum calcium level. It has, however, but a transient effect and is therefore suited only for tiding over an emergency such as a prolonged convulsion. Furthermore, if the tetany is of the eucalcæmic variety the beneficial effect of the increase in serum calcium may be almost immediately rendered null by the fact that little addition is made to the ionized fraction.

The second method, that of supplying vitamin D, is undoubtedly most satisfactory in all types where hypocalcæmia is the result of defective retention of lime. It takes some days, however, before the increased retention produced by vitamin D makes itself effective in raising the serum calcium. Accordingly, if there are active manifestations of tetany such as laryngismus or carpo-pedal spasm, some method must be adopted to tide over this latent period.

The supply of parathyroid extract would appear to be the ideal method of treatment where there is defective secretion of the parathyroid hormone, such as occurs after parathyroidectomy or in idiopathic hypoparathyroidism. Even in this type of case there are disadvantages. The preparation is expensive and, in addition, prolonged use of the extract leads to a weakening of its effect, due possibly to the development of an anti-hormone, so that larger doses have to be employed with diminishing effect. In infantile tetany due to vitamin D deficiency the use of this expensive preparation is neither necessary nor desirable. Its prolonged use, indeed, is contraindicated, since it produces its effect on the serum calcium by decalcifying osseous tissue.

The fourth method of raising the serum calcium by the use of acid-producing substances is also dependent on an increased flow of calcium from



the bones, and therefore should not be used for more than a few days when there is osteoporosis, unless steps are taken to make good the lime deficiency. This method has, however, one great advantage: not only does it lead to a rise in total calcium, but it also produces an increase in the ionized fraction so that it can be used in tetany of the eucalcæmic variety. Acid-producing substances can be given in therapeutic doses without risk to healthy children and to most infants and children with rickets. It has to be remembered that some children, particularly of the latter group, suffer from intestinal and other disorders that render them easily liable to disturbances of acid-base equilibrium so that a severe acidosis may be, and occasionally is, produced. This liability to acidosis is even more marked in the patient whose tetany is due to chronic interstitial nephritis. In this latter condition a small addition of acid may suffice to precipitate a very severe attack of uræmia.

These, then, are the methods in common use for raising the level of serum calcium and for the prevention and cure of the tetany syndrome. It will now be convenient to consider the treatment of each type of tetany in more detail.

**Rachitic Tetany.**—Efficient prevention and treatment of rickets is undoubtedly the best prophylactic. In this connection the biphasic effect of vitamin D on the retention of lime should be kept in mind. It has been shown by the writer and others that shortly after beginning the administration of vitamin D there may occur a rapid fall in the retention of calcium which may precipitate an attack of tetany. It is therefore advisable to make certain that ample calcium is available by giving large doses of an easily assimilable calcium salt (gluconate or lævulinate).

Once the signs of tetany are detected active treatment should be initiated as soon as possible. Calcium gluconate (10 c.c. of a 20 per cent. solution) may be given intravenously where the symptoms are urgent, *e.g.*, convulsive seizures or painful carpopedal spasm. If this degree of urgency is not required the gluconate may be given intramuscularly. It is doubtful whether even large doses of gluconate or lævulinate are efficacious when given by the mouth. If it is desired to avoid parenteral administration, 10 to 20 gr. (0.6 to 1.2 gm.) of calcium or ammonium chloride every four hours should be given. For tetany of the newborn a dose of  $7\frac{1}{2}$  gr. (0.5 gm.) suffices. This treatment depends for its effect on the fact that there is a net increase in acid ion in the body fluids. The calcium of the calcium chloride is retained in large part in the gut, while the ammonium ion is rapidly converted into the neutral urea, in both instances leaving an excess of uncompensated chloride ion to enter the tissue fluids. As has already been mentioned, the risk here is the production of a dangerous degree of acidosis, and great care should be taken to stop the drug before this develops. Thus vomiting, diarrhœa and increased depth or rate of breathing are indications for the prompt cessation of the drug. Even when these signs do not appear, the administration of calcium or ammonium chloride should not be continued for more than three days, from the very commencement of which vitamin D should be given in full therapeutic doses, or in one single massive dose (600,000 international units, as described on p. 408). The latter method has proved highly successful, leading to a cessation of convulsions almost immediately and to the disappearance of the spasmophilic state within two days.

When convulsions occur in rapid succession, and it is not feasible to administer calcium intravenously, it may be necessary to give a sedative. For this purpose chloral hydrate is generally satisfactory, although in very severe convulsive states chloroform inhalation may be required, but it must be emphasized that the use of these sedatives is a very temporary measure designed to act on the nervous system until the serum calcium is raised.

**Tetany associated with Coeliac Disease.**—Essentially this demands the same treatment as that outlined for the tetany of rickets. It is advisable, however, in view of the tendency to the passage of large bulky fluid motions to refrain from the use of acid-producing salts. The administration of calcium gluconate intravenously, intramuscularly or orally, depending on the urgency of the symptoms, and the institution of a low-fat diet with an adequate supply of vitamin D rapidly leads to a disappearance of the manifestations of tetany.

**Parathyroid Tetany** (considered in the section dealing with Parathyroid Disorders, see p. 435).

**The Tetany of Chronic Renal Disease.**—In this condition, which is due to the hypocalcæmia engendered in chronic renal disease, the difficulty of treatment lies in the very unstable acid-base equilibrium. The metabolism sways between the Scylla of alkalotic tetany and the Charybdis of acidotic uræmia. The administration of large amounts of alkali, while facilitating the urinary excretion of acid substances, reduces the ionized fraction of calcium. Nevertheless, renal function is in some cases so impaired that without the addition of alkali there is too great a call on the calcium stores of the body with resultant fall in the level of total serum calcium. On the whole, it is much better to make certain of a sufficient intake of alkali, since it is comparatively easy to deal with symptoms of tetany should they arise, whereas the acidotic state of uræmia is much more serious and likely to prove fatal. The best method of dealing with the tetany of chronic renal disease is the parenteral administration of calcium gluconate. Even after the symptoms have disappeared it is wise to continue the oral administration of this substance.

**Alkalotic Tetany.**—*Tetany due to Vomiting.*—This condition is the result of an alkalosis produced by the excessive loss of chloride in the vomitus. It is best dealt with by the injection of large amounts of sodium chloride as normal saline intravenously, subcutaneously or rectally depending on the severity of the vomiting. Rarely is it necessary to give any other medication, although calcium gluconate or ammonium chloride may be used. If the underlying cause is high intestinal obstruction, laparotomy may be necessary.

*Tetany due to Alkalis.*—In the alkaline treatment of pyuria and gastric ulcer, tetany occasionally supervenes. In these cases cessation of the alkaline medication usually suffices to remove the manifestations of spasmophilia. Only occasionally will it be necessary to give acid-producing substances such as ammonium chloride.

**Hyperventilation Tetany.**—This type is the result of alkalosis caused by overbreathing. The attack itself is rapidly alleviated by the inhalation of a gaseous mixture containing 5 per cent. CO<sub>2</sub>, 21 per cent. O<sub>2</sub> and nitrogen. This, however, is only a temporary remedy: the underlying causes of the hyperventilation should be removed if at all possible. In some, if not all instances, there is a very large neurotic element. Some form of psychotherapy is often helpful: the patient, who is usually highly strung, should

be told how the attacks are produced and encouraged to control the impulse to overbreathe. The use of sedatives such as phenobarbitone is often of considerable value.

### VITAMIN K DEFICIENCY

This vitamin, chemically a naphthoquinone, is found in green vegetables such as cabbage and spinach, and is said to be produced by bacterial activity in the intestine. It plays an essential part in the production of prothrombin so that any deficiency prolongs the clotting time of the blood and therefore increases the risks and dangers of hæmorrhage. It is doubtful whether after the neo-natal period there is any defect in the supply of this vitamin. In the early days of life, however, there is frequently some degree of hypovitaminosis K, presumably the result of defective transport across the placenta, the low concentration of the vitamin in milk and the absence of its synthesis in the intestine. In any case, the full-term infant has less than one-third of the adult proportion of prothrombin, while the premature infant has even less, and it seems certain that hæmorrhage in the newborn is the result of vitamin K deficiency.

In conditions where bile is absent from the small intestine, as in obstructive jaundice, vitamin K is poorly absorbed. Hypoprothrombinæmia may also occur in diarrhœal conditions such as cœliac disease, sprue and idiopathic steatorrhœa where fat absorption is defective, as well as in cirrhosis of the liver and other hepatic diseases.

The treatment of the vitamin K deficiency caused by these conditions is dealt with on p. 512.

### VITAMIN E

It is possible that the administration of this vitamin may prove of therapeutic value in cases of recurrent abortion (see p. 458).

N. MORRIS.

# DISEASES OF THE DUCTLESS GLANDS

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## THE THYROID GLAND

### SIMPLE GOITRE

**PROPHYLAXIS.**—In areas where goitre is endemic, prophylactic administration of iodine is carried out on a nation-wide scale. This is practised extensively in Switzerland, around the Great Lakes in the United States, and in other goitrous regions of the world. The results of such prophylaxis are good, and endemic goitre now ranks as one of the diseases which medical science has gone far to master. Though such prophylaxis is not practised in this country, some details of the iodine dosage necessary may be of interest, in view of the light shed on iodine requirements in general and in relation to the doses of iodine used in the treatment of thyrotoxicosis.

Two methods of iodine administration are practised: (a) The admixture of a small percentage of iodine with table salt, the exact proportion being fixed by law, to ensure that all members of the community ingest a sufficiency of the element; and (b) the administration of iodine to school children for a week or two in each year, and similar iodine therapy for women during pregnancy.

The amount of iodine added to salt is based on a knowledge of the quantity required per day by a human being. Estimates of this vary, but all agree that the amount is extremely low, somewhat less than 100 gamma per day (1 gamma = 0.001 mg.). Assuming an average daily salt intake of 10 gm., the addition of 1 part of iodine in 100,000 of salt will yield a daily intake of 100 gamma, which is ample for health. In actual practice the concentration of iodine added varies from 1 : 5,000 to 1 : 250,000 in different countries. It is probable that the higher concentrations are in excess of requirements.

Where iodine is given only over a short period in the year, the dosage is usually in the region of 0.2 gm. (3 gr.) of potassium iodide daily for ten days in autumn and spring. This represents a total yearly intake of 4 gm. potassium iodide, equivalent to about 3 gm. of iodine element, or an iodine intake of about 8 mg., or 8,000 gamma, per day, which is very much in excess of the amount given in iodized salt. Probably a good deal of the excess is lost by rapid excretion at the time of administration. The question arises as to whether excessive doses of iodine have any untoward effects. This will be discussed below (see next paragraph).

**Curative.**—The treatment of established simple goitre is less satisfactory than the results of prophylaxis. Prevention is once again better than cure. Administration of iodine is worthy of trial, and may prove successful, but diminution in the size of the gland is by no means the rule. Continental and some American writers are insistent on the danger of provoking hyperthyroid symptoms by the ingestion of excessive quantities of iodine (Iodine-Basedow). In Vienna the fear of this complication is so great that it is unusual to prescribe potassium iodide for arteriosclerosis or in cough

mixtures, and our reckless administration of potassium iodide to such cases in 15-gr. (0.9 gm.) doses provokes consternation. Physicians in this country, who see relatively few cases of simple goitre, can hardly judge whether this is a common complication, but general opinion here is against its frequency. The existence of Iodine-Basedow is also denied by some American observers who work in areas of high goitre endemicity, where iodine is given freely. Means quotes an impressive array of syphilitic cases in such an area, all receiving massive doses of iodide, without a case of hyperthyroidism occurring amongst them.

The dosage of iodine given in cases of simple goitre is governed then by our beliefs regarding the reality of Iodine-Basedow. In Switzerland, where such belief is strong, an additional ration of 10 mg. iodine per day is given to established cases of simple goitre. In Britain, where the menace is regarded lightly, the usual dose is of the order of 0.1 to 0.2 gm., usually in the form of Lugol's solution, M<sub>xv</sub> to M<sub>xxx</sub> (0.9 to 1.8 c.c.) per day.

When iodine fails to effect improvement, as it so often does, thyroid extract is sometimes tried. It is difficult to understand the rationale of its administration unless symptoms of subthyroidism are present. The results of thyroid treatment on the size of the gland are disappointing.

The majority of simple goitres yield only to surgical treatment. This is not indicated in the average mild case in a young subject, but should be considered if pressure symptoms arise, if the swelling is disfiguring, if the gland becomes nodular, if hyperthyroid symptoms develop, or if any suspicion of malignant change arises. It should be remembered that a large proportion of simple goitres eventually become adenomatous, and about 25 per cent. of adenomatous goitres become toxic. Thus the prophylaxis of simple goitre and the surgical removal of non-toxic adenomatous goitres constitute the prophylaxis of thyrotoxic adenomata.

### CRETINISM

The successful treatment of cretinism depends upon its early diagnosis and the adequate administration of thyroid throughout the lifetime of the patient. As cretinism in this country is sporadic and rare, it is much more likely to escape detection in its early stages than in countries where it is endemic and relatively common. The untreated cretin, over two or three years of age, presents a classical clinical picture, but during the first year of life, when adequate treatment offers the most favourable prognosis, the physical signs are much more equivocal.

The brain of an infant develops with great rapidity during the first year of life and an absence of thyroid secretion during this critical period will almost certainly result in permanent damage, but if continuous adequate treatment is started between the third and sixth month of life there is an excellent chance of entirely successful mental development. As diagnosis is rarely made until much later, however, only a small percentage of cretins grow up mentally normal. The majority remain more or less retarded with an intelligence quotient of below 70 per cent., the extent of the mental defect depending largely on the length of time which elapsed before the start of treatment. Although early treatment is essential if full mental development is to result, a cretin may remain untreated until the age of four and yet show skeletal growth to almost normal proportions under proper treat-

ment. The administration of thyroid to untreated cretins over the age of twelve is often worse than useless. Usually it only succeeds in transforming an imbecile who is placid and static into one who is peevish and unmanageable.

The quantity of thyroid required is usually gauged by the response of the patient. The correct dose is that which will allow of normal growth and development without producing signs of hyperthyroidism. The amount required varies with the age and weight of the child from about  $\frac{1}{10}$  gr. (6.5 mg.) daily in early infancy to doses of 1 to 3 gr. (0.06 to 0.18 gm.) daily in late childhood. (All references are to the B.P. preparation, thyroideum. This is a dried extract, standardized to contain 0.1 per cent. of iodine in combination as thyroxine. Non-official preparations vary considerably in potency, and unless this is stated by the manufacturers in terms of the B.P. standard, such preparations should not be used.) A very small dose is sufficient to banish the grosser stigmata of cretinism and to effect a remarkable improvement, but the practitioner should not be content with the mere disappearance of symptoms, since a dose sufficient to dispel symptoms may be inadequate to ensure satisfactory growth and osseous development. The rule which should govern the administration of thyroid in cretinism is quite different from that in adult myxœdema, in which the smallest dose that will suffice to keep the patient free from hypothyroid symptoms should be given. In cretinism the largest dose consistent with freedom from thyrotoxic symptoms should be administered. The toxic symptoms to be noted are excessive irritability, diarrhœa, muscular twitchings, undue loss of weight, sweating, tachycardia and pyrexia. Just as in the treatment of heart failure by digitalis, so the dose of thyroid should be built up until mild toxic symptoms appear, and then, after a few days' freedom from treatment, a maintenance dose just below the toxic level should be given. The initial dose of thyroid should nevertheless be small, since subthyroid cretins are much more sensitive to thyroid medication than those whose metabolism has been raised to normality by appropriate treatment. A large initial dose in an untreated case may result in alarming toxic symptoms. It should be remembered also that it takes fully a month for a daily dose of thyroid to exert its maximum effect. The dose should not therefore be increased until this period has elapsed. The patient's growth and osseous development should be checked by careful measurements, and by an X-ray examination every six months. Inadequate development is usually due to inadequate dosage. It cannot be too strongly emphasized to the parents that it is necessary to continue the daily administration of thyroid throughout the life of the patient. The dramatic improvement, which results from properly controlled treatment, is apt to encourage the belief that permanent "cure" has resulted, and that treatment can be discontinued.

### MYXŒDEMA

**Juvenile Myxœdema.**—Sometimes a clear distinction is not made between cretinism and juvenile myxœdema: in cretinism the thyroid is deficient from birth; in the latter it becomes deficient after a number of years in which mental and physical development have progressed normally. The prognosis is much better than in cretinism, as permanent damage to the central nervous system is not so apt to result from a deficiency of thyroid

secretion in later childhood or adolescence as it is from a similar deficiency during the critical months of infancy.

As in cretinism, dosage with thyroid should be the maximum consistent with the avoidance of toxic symptoms. From  $1\frac{1}{2}$  to 3 grains (0.09 to 0.18 gm.) will usually suffice for maintenance treatment, but a smaller initial dose is indicated. Severe thyrotoxic effects, even including temporary psychoses, may occur if full dosage is given straight away to markedly sub-thyroid patients. Again, treatment should be continued throughout life, and should be regulated during the years of growth by frequent measurements and radiological examinations to ensure that osseous development is proceeding normally.

**Adult Myxœdema.**—There are few conditions in which the response to treatment is so gratifying as in hypothyroidism in the adult. The simple oral administration of thyroid will relieve symptoms entirely: within a week of starting treatment the patient's appearance improves; the speech is clearer and the mental functions brighter; cold is felt less, the appetite improves and constipation is relieved; and some loss of weight occurs, principally owing to free diuresis to be followed by a gain in weight due to improved nutrition. It usually takes some weeks or even months for the skin, hair and blood picture to become normal, and in the case of the latter it may be necessary to administer iron in addition to thyroid. There is ample evidence to show that longevity and myxœdema are by no means inconsistent, provided the latter is properly treated.

The aim of treatment in myxœdema is to give a daily dose of thyroid sufficient to rid the patient of symptoms. Nothing is to be gained by raising the metabolic rate to an arbitrary standard of normality if symptoms can be eradicated at a lower level, for elderly hypothyroid patients will often develop undesirable symptoms if their metabolism is raised to normal or only a little over it. The practitioner should not feel that an inability to carry out basal metabolic rate determinations need militate against his successful treatment of hypothyroid states: in adult myxœdema the symptoms of the patient should be his guide; in infantile and juvenile hypothyroidism, when a basal metabolic rate determination would be more valuable, it is usually impracticable, even in hospital. There is no way of determining in advance the *exact* dose of thyroid for an individual case of myxœdema, but the response to thyroid is on the whole less variable than with most other drugs in the treatment of other conditions. Means has estimated that half a grain (0.03 gm.) a day will raise the metabolism of a completely myxœdematous patient with a basal metabolic rate of between  $-30$  and  $-40$  to about  $-20$ ; one grain (0.06 gm.) to about  $-10$ ;  $1\frac{1}{2}$  grain (0.09 gm.) to about  $-5$ , and 3 grains (0.18 gm.) to approximately  $\pm 0$ . It will be noted again that the more hypothyroid the patient, the more sensitive he is to thyroid. The majority of patients are free from symptoms, and feel well with a maintenance daily dose of  $1\frac{1}{2}$  to  $2\frac{1}{2}$  grains (0.09 to 0.15 gm.). It is seldom necessary to give more than 3 grains (0.18 gm.) a day. In any case, it is wise to start with a small dose of  $1\frac{1}{2}$  grain (0.09 gm.) a day, especially for elderly patients suspected of coronary disease. The dose can be gradually raised at intervals of a month until a satisfactory response is obtained. In this way there is less danger of producing cardiac complications in susceptible cases.

The untreated myxœdematous patient has a dilated heart and a low

blood pressure. Owing to the slow rate of metabolism, however, actual cardiac decompensation is rare, and it is unusual to find either the subjective or objective manifestations of congestive failure. Degenerative changes in the coronary arteries are common, possibly due in some degree to the hypercholesterolaemia characteristic of the condition, and when the metabolism is raised under treatment, and improvement occurs in the tone and action of the heart, anginal symptoms may occur. The sclerosed coronary vessels may have been adequate to maintain a sufficient blood supply to the sluggish myxoedematous myocardium, but quite inadequate for the brisker circulation induced by thyroid. In such cases the practitioner has to steer a careful course between the persistence of myxoedematous symptoms on the one hand and the occurrence of angina on the other. When angina is a marked feature he may have to be content to relieve only the grosser symptoms of myxoedema, and to maintain the metabolism at about -20 by the prescription of as little as half a grain (0.03 gm.) of thyroid daily.

### HYPERTHYROIDISM

The treatment of thyrotoxicosis has advanced greatly during the last twenty years. Practically the only treatment before that time was rest, sedatives, and the continuous administration of iodine, to which drug the patient soon became largely or completely refractory. It is true that many mild cases in young girls cleared up spontaneously on this régime, particularly if a satisfactory solution could be found to domestic worries, unhappiness at work or an affair of the heart. A proportion of more severe cases also eventually burnt themselves out after a greater or less number of years, during which their semi-invalid existence was a misery to themselves and their associates. A large number died from progressive heart failure with auricular fibrillation, or in thyrotoxic crisis often precipitated by an infectious illness. Occasionally, after a physician had battled unsuccessfully with a patient for many years he would refer her practically *in extremis*, as a last desperate resort, to a surgeon. The result, which was almost invariably fatal, confirmed the physician in his complacent belief that surgery should play no part in this disease.

All this was changed when the proper pre-operative use of iodine was introduced by Plummer. This, combined with improved operative and, particularly, anæsthetic technique, reduced operative mortality in the hands of surgeons specializing in this operation to under 2 per cent. High mortality figures still occurred when late or neglected cases were referred for operation, or when the surgeon was unpractised in the art of goitre surgery.

The results of good medical and surgical co-operation in this sphere are as gratifying as any in the whole range of therapeutics. Improvement is usually dramatic within a few days of operation, and the total period of disability, from the pre-operative period till the patient is fit to return to work, averages from three to four months. The mortality over all is certainly under 5 per cent., and the recurrences after operation are probably not much more than 5 per cent.; the remaining 90 per cent. are rid once and for all of their disorder, though a few become myxoedematous—a condition readily amenable to simple treatment.

The last twenty years thus constitute a surgical era in the treatment of thyrotoxicosis in which the results have been infinitely superior to those



of the purely conservative one which preceded it. It is probable that the wheel is now going to complete a full circle and that we, armed with a new and potent drug in the form of thiouracil, are about to start a new medical era which will in its turn supersede the surgical one to some extent.

At the time of writing, it is still too early to be entirely dogmatic about the indications for thiouracil treatment as opposed to thyroidectomy in the management of thyrotoxicosis. It is probable, however, that most cases—certainly young people suffering from primary thyrotoxicosis—should be given a trial with thiouracil before resorting to surgery. The writer's experience suggests that surgery should be reserved for the following cases:—(a) patients with large unsightly goitres, particularly if pressure symptoms are present, since thiouracil is unlikely to effect a significant reduction in their size; (b) all those with a retrosternal goitre, since thiouracil may occasionally increase the size of a goitre and in retrosternal cases may thus give rise to serious pressure symptoms, (c) those few cases of primary thyrotoxicosis which after a trial with thiouracil are found to be drug resistant, or which show toxic reactions to it. It is also probable that thyroidectomy is the method of choice in patients with secondary (nodular) toxic goitres associated principally with cardiovascular signs and symptoms. Thiouracil will undoubtedly benefit the great majority of such cases, and is preferable to thyroidectomy in old as opposed to middle-aged patients, but it is less successful than surgery in the completeness and permanence of its curative effects in such circumstances. We must also take into account the patients' own wishes on the subject after we have made them conversant with the pros and cons of medical as opposed to surgical treatment. Some patients will resent the necessity of having to continue to take a drug for a long period of time and possibly permanently, and will prefer surgical intervention with the strong expectation which surgery brings of being finished with their disorder once and for all. Such a wish on the patient's part must be given due consideration by the doctor.

**General Management.**—Certain general measures are applicable whether thiouracil is used or whether the patient is being prepared for thyroidectomy by pre-medication with iodine.

*Rest.*—An initial period of rest is nearly always desirable. In mild cases it is probably sufficient to arrange that the patient does not rise till after breakfast, has two hours' rest in bed or on a couch after lunch, and retires to bed in the early evening between 7 and 8 P.M. In more severe cases rest in bed is essential, especially for a week or two at the outset.

During this period of conservative treatment every effort should be made to find the cause for the development of hyperthyroid symptoms. Unhappiness at work or in the home, an unhappy love affair, the fear of an undesired pregnancy in a young woman, or some similar psychological disturbance may be discovered in the course of investigation, and may be dealt with. In many cases the doctor is powerless to interfere in respect of such matters even if they be elucidated; but in others a doctor's advice may be invaluable. In the discovery of the cause of the disorder, and in exercising his tact and judgment in its elimination, the family doctor, who enjoys the confidence and trust of his patient, can often render service beyond the scope of the hospital specialist. When the environment at home is obviously at fault, as it so often is in these cases, it is important to advise hospital treatment at the outset, and it may be necessary to prohibit visitors and letters.

The attainment of mental rest is facilitated by the use of sedatives, of which one of the most effective and probably the most convenient is phenobarbitone. It should be given in doses of  $\frac{1}{2}$  to 1 gr (0.03 to 0.06 gm.) twice or thrice daily, according to the individual tolerance to the sedative, which varies greatly. The drug may be given for long periods of time.

*Diet.*—During this period the diet should be generous, and in most cases unrestricted in variety. The increased metabolism of the body demands a fuel intake in excess of that usual for people of the same age and sex and build. A total calorie intake of at least 2,500 to 3,000 is desirable. Carbohydrate and fat are allowed *ad libitum*, but protein should not exceed 100 gm. per day. Protein in fair quantity is required to make good the tissue waste inevitable with high metabolism, but excessive protein intake is undesirable, since its specific dynamic action tends to raise still further the already excessive metabolic activity. The increased calorie intake is most simply obtained by giving additional feeds of fruit juice and glucose, switched egg, milk or proprietary foods such as Ovaltine or Horlick's, which can be interspersed between the principal meals and given last thing at night.

Increase in weight is always a reassuring and satisfactory sign. It is a sound plan in all cases of thyrotoxicosis, even in those in which symptoms have apparently subsided and in which the disease is regarded as "cured," to make the patient keep an accurate weekly record of body-weight. In active cases an increasing weight is a valuable sign of improvement; in quiescent cases, a stationary weight is equally reassuring. In all cases, a fall in weight of even a few pounds, especially if steadily maintained week by week, is disquieting, and is the signal for a review of the whole treatment of the case.

*Septic Foci.*—Many cases of thyrotoxicosis are noted to follow acute infections, and this observation has led to debate as to the possible rôle of sepsis in aggravating the symptoms of the disease. In some patients obvious septic foci are present, particularly in the upper respiratory tract (accessory sinuses, tonsils) or in the teeth (pyorrhœa, apical abscesses). Removal of such foci is frequently advocated as a preliminary to a course of medical treatment, and is even demanded by some surgeons before they will undertake operation on cases of hyperthyroidism. However desirable it may be to get rid of such foci, there is no doubt that their removal is fraught with danger in all but mild cases. It is not sufficiently appreciated that tonsillectomy and similar operations carry nearly the same risk of post-operative hyperthyroid crisis and death as the major operation on the thyroid gland itself, and an extremely high mortality follows acute abdominal operations in such patients. Pre-operative preparation with thiouracil should therefore be undertaken whenever possible until all hyperthyroid signs and symptoms are well controlled before septic foci are removed. This will usually involve treatment for about two months. In those cases in which treatment by thiouracil is contraindicated the removal of septic foci should be postponed until the thyrotoxic state has been abolished by partial thyroidectomy.

*Thiouracil.*—*Pharmacological Action.*—In 1942 it was discovered that thiourea and its derivatives—of which thiouracil is the most active—produced goitres when fed to experimental animals. The changes in the thyroid were those of a diffuse hyperplasia with a decrease of colloid in the follicles, and were indistinguishable from the changes found in a thyrotoxic gland.

Paradoxically, however, this thyroid hyperplasia was associated, not with hyperthyroidism in the animal, but with myxœdema. This association of thyroid hyperplasia with hypothyroidism could not be explained on the basis that the goitrogenic substances neutralized thyroxine in the body tissues, since the administration of thyroid extract or thyroxine entirely nullified their action. Further work showed that the antithyroid substances produced their effect by interfering directly with the synthesis of thyroid hormone, probably by preventing the iodination of tyrosine. As the hyperplasia of the thyroid did not take place if hypophysectomy had been carried out previously it was clear that the goitre was mediated through the anterior pituitary which was stimulated by the myxœdematous state of the animal to produce thyrotropic hormone in excess, and hence thyroid hyperplasia. Our present knowledge derived from experimental work may be summarized briefly as follows: Thiourea derivatives→Prevention of iodination of tyrosine→Lack of thyroid hormone→Lowered metabolism→Compensatory increased production of thyrotropic factor from the anterior pituitary→Thyroid hyperplasia.

*Dosage.*—The prevention of thyroxine synthesis is not an all-or-nothing reaction, and a relationship exists between the dose of antithyroid substance and the degree of hypothyroidism produced. The aim in hyperthyroidism is to decrease the synthesis of thyroxine to a normal level but not below it, so that the pituitary will not be stimulated to produce thyroid hyperplasia.

Thiouracil is given by the mouth in tablet form and is rapidly absorbed and excreted in the urine. When 0.6 gm. is given daily an equilibrium is soon reached between the concentration of the drug in the blood and its excretion in the urine. A larger dose does not increase the concentration in the blood to any significant extent as the excess is immediately excreted in the urine. Therefore for initial treatment, in order to bring the patient under the full influence of the drug, 0.2 gm. is given three times a day.

Once a significant effect has been produced by this initial treatment the dose is reduced to a maintenance one, since a continuation of the high initial dosage would produce myxœdema and the indirect effect of enlargement of the goitre through over-production of thyrotropic hormone from the pituitary. The optimum maintenance dose varies from case to case. The writer usually employs a daily dose of 0.2 gm. to begin with, decreasing this after a month or two to 0.1 gm. and finally to 0.05 gm. In mild cases 0.1 gm. instead of 0.2 gm. may be given as the initial maintenance dose. Should there be any sign of a return of thyrotoxic symptoms the maintenance dose should be appropriately increased.

Some authorities claim that methyl thiouracil in similar dosage is less toxic and more effective than thiouracil itself. The writer is not convinced that there is any significant difference between the two drugs in these respects, but as methyl thiouracil is slightly cheaper it is probably the better drug to use. Recent reports have suggested that propyl thiouracil is the drug of choice both as regards effectiveness and lack of toxicity. At the time of writing, however, there has been insufficient experience of its clinical trial to justify its general use. Doses of 25 to 50 mg. a day are used.

*Clinical Effects.*—A normal human subject may be given thiouracil for months without producing hypothyroidism or goitre. This is to be expected since the rate of metabolism will remain constant as long as the store of

thyroid hormone in the gland is adequate to supply the organism. It is only when the store is exhausted that the decreased rate of hormone synthesis becomes apparent, and in the normal gland large stores are present. Since, however, the store of thyroid hormone in hyperthyroid glands is very small, an effect is produced by thiouracil in thyrotoxic cases within a few days.

The effects of thiouracil are on the whole fairly precise and predictable. For a few days no result is observed, but by the end of about a week some subjective improvement occurs, the sweating and flushing of the skin being usually the first symptoms to be ameliorated. Thereafter all the thyrotoxic symptoms steadily improve, the improvement being significant in three or four weeks and maximal at the end of about two or three months. The objective and measurable signs of thyrotoxicosis parallel the subjective sensations of the patient in their improvement.

The blood cholesterol concentration is low in untreated hyperthyroidism just as it is high in myxœdema. On the average it rises under the influence of thiouracil, but it is not a reliable yardstick for the control of treatment since in individual cases there is often little correlation between the blood cholesterol concentration and the progress of the case.

After a latent period of about ten days a fall in the B.M.R. becomes noticeable, and on the average this fall reaches significant proportions in about three weeks' time. The B.M.R. is a clinical test which is often endowed with almost mystical potentialities by those with little experience of it. Actually it is a procedure which lacks universality of application in ordinary practice and is certainly not one which shou'd be attempted on out-patients without admitting them to hospital for a night or more if accurate results are to be obtained. Even in hospital many patients become over-anxious about their B.M.R. readings and in consequence artificially high estimations are obtained. The effect of thiouracil on the B.M.R. is on the whole so precise and invariable as to make B.M.R. readings superfluous in ordinary practice. The initial dose of thiouracil can be confidently reduced to a maintenance one in from three to four weeks, as experience has shown that the B.M.R. usually approaches normality at this time.

A gain in weight is a characteristic effect of thiouracil treatment. This generally starts shortly after the commencement of treatment and is often a very striking, and occasionally even an embarrassing, result of therapy. As has been said, the weight is one of the best prognostic guides in hyperthyroidism.

Thiouracil does not act uniformly on all the signs of thyrotoxicosis, and the last to show improvement is, on the whole, the associated tachycardia and high pulse pressure. When a marked degree of tachycardia exists its control is often delayed long after the B.M.R. has fallen to normal and the weight and other signs and symptoms have greatly improved. Patience, therefore, has sometimes to be exercised in this respect.

In some cases auricular fibrillation due to thyrotoxicosis returns to normal rhythm under the influence of thiouracil, just as normal rhythm may occur spontaneously after thyroidectomy. In a number of cases, however, the fibrillation persists in spite of satisfactory control of the other features of hyperthyroidism by thiouracil, just as it may persist after thyroidectomy, and quinidine treatment may be necessary following full digitalization to restore the rhythm to normal (see p. 664).

The mild diabetic state so commonly associated with thyrotoxicosis may often be cured by thiouracil just as it may be cured by thyroidectomy. There are, of course, other thyrotoxic cases with true severe diabetes, and such diabetes is not cured, though it may be ameliorated, by thiouracil or thyroidectomy. In these latter cases dietetic and insulin treatment must be instituted, as described on p. 343.

The exophthalmos is often not materially benefited by thiouracil treatment. Slight improvement in this feature is commonly noted, and in a few cases this may be marked. The same remarks apply to thyroidectomy.

On the whole, also, thiouracil in the dosage used does not greatly influence the size of the goitre. Slight fluctuations in size may be noted from week to week and month to month. A fairly constant feature is the increase in the size of the gland coincident with the menstrual period, and a recession after it. Almost invariably the goitre becomes softer in contrast to the firmer gland produced by iodine. Occasionally the gland becomes definitely smaller, and, in some cases in which the thyrotoxic tendency has been abolished by thiouracil and it has been possible to give up the drug altogether, the size of the gland may diminish very materially.

Theoretically it would seem that if the pituitary is stimulated by *overdosage* with thiouracil to produce excess thyrotropic hormone an increase in the size of the goitre will occur similar to the hyperplasia produced in experimental animals. This certainly occurs when a patient is overdosed with thiouracil, and several cases have been recorded in which very large goitres have been produced in this way. A serious increase in the size of the gland, especially when it is associated with myxœdematous signs and symptoms, is therefore an indication of overdosage.

*Drug Resistance.*—Occasionally patients are found who seem for no apparent reason to be resistant to thiouracil. These cases are, however, most exceptional. A patient should certainly not be labelled drug resistant simply on account of the persistence of tachycardia and high pulse pressure during the first few weeks of treatment. As has been said earlier, it may take a long time before these features of thyrotoxicosis are abolished by thiouracil.

*Toxic Effects.*—Like most potent modern drugs thiouracil is a two-edged weapon, which though capable of much good may also give rise to very serious toxic reactions. It is most important that the practitioner should be familiar with and be on the outlook for the toxic effects of the drug before starting treatment. The recorded signs of toxicity are fever, enlargement of lymph glands, rashes, conjunctivitis, swelling of the legs and feet, leucopenia, granulopenia, thrombocytopenia and acute sensitivity reactions consisting of high temperature and vomiting. Of these the serious signs calling for a cessation of treatment are the blood changes and the acute signs of sensitivity. The slight œdema of the ankles and feet which may be noted is unassociated with cardiac failure or renal damage, and disappears though treatment is continued. Serious blood dyscrasias are most likely to occur during the initial period of treatment and are comparatively rare once the dosage has been reduced to the small quantity necessary for maintenance treatment. During the three or four weeks, therefore, in which the high initial dosage is being given, it is ideal for regular white blood counts to be undertaken, and if the count falls below 3,000 the drug should be stopped. The agranulocytosis, however, may occur so

rapidly that very frequent white blood counts would have to be made in order to recognize the tendency at an early stage, which is usually impossible in ordinary practice. Patients should, therefore, be warned to stop taking the drug and to report to the doctor should any untoward symptoms arise and particularly on the first sign of a sore throat. Provided they do this at once the likelihood of serious toxic reactions is not such as to make thiouracil an unsuitable drug for use in general practice, and when the thyrotoxicosis is mild the patients may be treated successfully from the outset as ambulant cases. The frequency with which toxic reactions occur tends to diminish the longer the patient has been taking the drug. Agranulocytosis, especially, is rarely encountered once the first two months of treatment have been successfully surmounted.

*Ultimate Effects of Thiouracil.*—It is too early yet to make any dogmatic statement on what the ultimate effect will be of thiouracil treatment. It is clear that a maintenance dose must be continued for a long time, for if it is discontinued after less than a year's treatment a gradual return of thyrotoxic signs and symptoms takes place in a high proportion of cases. It is unwise to stop the use of the drug unless it has been found possible to control completely all thyrotoxic signs and symptoms for some months with a maintenance dose of as little as 0.05 gm. a day. There are theoretical grounds for believing that ultimate complete cure may result in at least a proportion of cases, for we know that long continued hyperplasia may ultimately give way to atrophy of the thyroid, and if we can tide the patient over till this occurs the state of thyrotoxicosis may be cured. Further, primary thyrotoxicosis at least is certainly a psychosomatic disease in which the excessive endocrine activity has a disastrous effect upon the psychological state which in its turn exacerbates the endocrine disease. If this vicious circle can be broken for a time, either on the psychological side or on the endocrine side, hopes of complete cure may be entertained. There seems reason to believe that these theoretical expectations may receive practical clinical confirmation. A number of the writer's patients, after taking thiouracil for periods of time varying from one to two years, have been able to give it up altogether, and the thyrotoxic signs and symptoms have remained in abeyance for over two years, so as to justify the expectation that they have been permanently abolished. A proportion of cases, however, have shown a gradual return of thyrotoxic symptoms necessitating a resumption of treatment.

*Summary.*—There can be no doubt that we possess in thiouracil a drug with great potentialities. It can be given to patients suffering from thyrotoxicosis with the virtual certainty that after a short latent period improvement will occur. The initial dose should not be larger than 0.6 gm. daily, and this should be administered for at least three weeks, and not longer than four weeks, when a maintenance dose should be given. The maintenance dose varies from 0.2 gm. to 0.05 gm. daily. After a prolonged period of maintenance treatment lasting not less than a year a proportion of cases may be permanently cured and may be able to abandon the use of the drug without a return of thyrotoxic signs and symptoms.

*Iodine.*—The alternative treatment to thiouracil is partial thyroidectomy. As has been said, this operation should now be reserved for those few cases who are resistant, or show toxic reactions, to thiouracil; for cases with large unsightly goitres, or with retrosternal goitres; and possibly for

middle-aged patients with nodular goitres in whom cardiovascular signs and symptoms are the predominating features.

There is still some doubt as to whether thiouracil or iodine should be used to prepare the patient for thyroidectomy. Each has its advantages and disadvantages. Iodine seldom restores the metabolism of a severe case to normal, and, though it greatly improves thyrotoxic signs and symptoms, it only ameliorates them to a greater or less extent and does not hold them in complete abeyance as is usually the case with thiouracil. Further, there is a crucial moment to operate upon a patient who has been given iodine—between the seventh and the fourteenth day. If that moment is missed, owing perhaps to the patient developing a respiratory infection, it is necessary to wait for two or three months and to start all over again, for it is dangerous to operate upon a patient when the B.M.R. is on the up-grade. With thiouracil the effect is permanent as long as the administration of the drug is continued, and any convenient date can be chosen for operation. On the other hand there seems little doubt that the thyroids of patients prepared for operation by thiouracil are more vascular than those prepared by iodine. Further, in a few cases thiouracil may lower the white blood count of the patient, thereby rendering her more liable to post-operative infections. Thus, for those patients who do not show toxic reactions to thiouracil, the ideal pre-operative treatment probably involves the use of both drugs. Thiouracil is given for a month in full dosage until all thyrotoxic signs and symptoms are controlled. Its administration is then stopped and iodine is given for the ten or fourteen days immediately preceding the operation.

The mode of action of iodine is entirely obscure, and the details of its effects are still in dispute, but there is no doubt that it does cause remission of symptoms. It continues to be widely prescribed in the familiar Lugol's solution. This contains a mixture of iodine (5 per cent.) and potassium iodide ( $7\frac{1}{2}$  per cent.) in water. The iodine content of potassium iodide is approximately 75 per cent., so that the total iodine content of Lugol's solution works out at approximately 10 per cent. On this basis 10 minims (0.6 c.c.) of the solution contain the equivalent of 1 gr. (0.06 gm.) of iodine. There seems no valid reason for prescribing iodine in this cumbersome form, exactly similar results being obtained by giving potassium iodide in appropriate doses: in fact, the substitution of potassium iodide for Lugol's solution in practice is long overdue. The dosage of potassium iodide required in cases of hyperthyroidism is small by ordinary expectorant or antiluetic standards, and the substitution of 10 or 15 gr. (0.6 or 0.9 gm.) doses for an equal number of minims of Lugol's solution is liable to give rise to unpleasant symptoms and is not without danger. A usual dose of potassium iodide in cases of thyrotoxicosis is 1 gr. (0.06 gm.) twice daily. The drug may be prescribed conveniently in a solution containing 1 gr. (0.06 gm.) to the fluid drachm (3.6 c.c.) flavoured as desired.

The iodine content of this dose has been shown to be considerably in excess of the quantity required for full iodine effect. It appears from the careful work of Means, Lerman and others that 6 mg. of iodine daily produces the maximum effect on pulse-rate, B.M.R., and symptoms. This quantity of iodine is contained in about 1 minim (0.06 c.c.) of Lugol's solution per day. The larger doses commonly employed do no harm, provided their use does not lead the physician into the fallacy of believing that



90 minims (5.2 c.c.) per day will produce a more dramatic effect than 5 or 15 minims (0.3 or 0.9 c.c.) a day.

Whatever be the mechanism of iodine action it appears to run a definite time-course. The action is at its height in from ten to fourteen days, the B.M.R. showing an initial sharp fall which diminishes in its steepness as the low B.M.R. level is approached. The dose of iodine, provided it is over 6 mg. per day, appears to exert no influence either on the steepness or the depth of the fall. During this period of falling B.M.R. there is a marked decrease in the intensity of all symptoms, with a gain in weight, and a slowing of the pulse-rate. The latter naturally is not to be expected in cases with auricular fibrillation. This iodine response occurs in the great majority of cases, though now and then a patient fails to respond in the classical manner.

Opinions differ as to the course of the disease when iodine administration is prolonged beyond the ten to fourteen day period. In general, the opinion of physicians and surgeons is that the pulse and B.M.R. start to rise again, the symptoms become aggravated, and a general deterioration in the patient's health occurs. Such a patient is considered to have escaped from iodine control and to be refractory to further dosage. There is no doubt that such deterioration under iodine frequently occurs in cases allowed to go on taking the drug after the first ten to fourteen days. Means and Lerman, however, consider that such cases are not really iodine-resistant, but are still under the control of iodine though their state grows worse. The disease is known to pursue a cyclic course, and it is claimed that such cases may be on the up-grade of a cycle of activity during the period of observation. If iodine be stopped when such a case is growing steadily worse there is a sharp acceleration of the deterioration, which is claimed to represent the escape from iodine control consequent on the cessation of the administration of the drug. Iodine is considered to hold the symptoms and B.M.R. in check at a level somewhat below that which they would attain in the uniodized case.

The question of iodine resistance is of considerable practical importance, since pre-operative preparation with iodine is so important. There is no doubt that when operation is contemplated the first abrupt fall in the B.M.R., etc., should be the signal for carrying out the operation. The difficulty arises in the pre-operative management of cases who have been treated medically with iodine for prolonged periods. If iodine resistance is considered to be real and not imaginary, then the patient should be sent away *without* iodine for a period of two to three months before operation. At the end of this period iodine refractoriness will have disappeared and the drug may be restarted and operation carried out as in the freshly iodized case. On the other hand, if it is believed that the climbing B.M.R., etc., under iodine does not denote iodine escape but a natural cycle of activity, then the giving of the drug should be continued, secure in the knowledge that the peak of the crisis will be lessened by its control. Operation may then be carried out when the crisis of the cycle has passed and the metabolic rate is once more upon the down-grade. Evidence at the moment is not conclusive, but it is safe to say that, in general, surgeons prefer freshly iodized cases and will not operate on patients who have taken iodine for prolonged periods unless an iodine-free period of six to eight weeks has elapsed immediately before the pre-operative iodine preparation.



**Pre-operative Treatment.**—Careful medical preparation is an essential preliminary to operation. The patient should if possible be in the hospital or nursing home in which the operation is to be performed, though preferably not in the surgical ward. The date of the proposed operation should be left indefinite to the patient. Complete rest in bed should be maintained and phenobarbitone or other sedative should be administered. Visitors should be few and every measure taken to ensure that the patient is mentally at ease. A generous diet of the type already described (p. 425) should be allowed, with the addition in the few days before operation of glucose and orange juice (4 oz. of orange juice with  $\frac{1}{2}$  oz. of added glucose) once or twice daily. Not uncommonly diabetes occurs along with thyrotoxicosis, and in cases with glycosuria, therefore, blood-sugar analyses should be carried out. These will decide whether the condition is simply due to the hyperthyroidism or whether a true diabetes mellitus is present. In the latter event treatment should be modified accordingly (see p. 343).

Digitalis is of no value in cases with simple tachycardia without failure and should not be given. Its use in cases with fibrillation is discussed below. Iodine should be given, preferably as potassium iodide in doses of 1 gr. (0.06 gm.) twice a day, for ten to fourteen days before operation, when the pulse and B.M.R. will have fallen to a new low level and the most favourable moment for operation occurs. The general state of the patient leaves no doubt as to the improvement, of which the low pulse-rate and B.M.R. are merely reflections. Estimations of the B.M.R. are a luxury, and need not be carried out if careful attention is paid to the bedside signs of pulse, weight and general well-being. Explanation to the patient that the improvement which she feels indicates that operation is now safe will help to allay the apprehension with which many regard the ordeal.

*Pre-operative Treatment with Cardiac Failure and Auricular Fibrillation.*—The pre-operative treatment of a case with congestive failure and auricular fibrillation does not differ, so far as the thyrotoxicosis is concerned, from that of an uncomplicated case. The congestive failure should, however, be treated along the usual lines with digitalis and diuretics, salt and fluid restriction (see p. 631). It will often be found that relatively larger doses of digitalis are required to control the ventricular rate in cases of fibrillation with hyperthyroidism than in those of other ætiology, probably on account of the increased rate of destruction of the drug. Operation should be undertaken only after adequate control of the failure, at a precise time dictated by the hyperthyroid condition. Digitalis should be maintained right up to the day of operation, and should be continued in the post-operative period. It is not good practice to attempt to restore normal rhythm by means of quinidine before operation, for even if this be successful, the resumption of normal rhythm deprives digitalis of its chief action in controlling the ventricular rate and robs the physician of his main weapon against excessive tachycardia. In any case, patients so restored to normal rhythm often relapse into fibrillation at operation or during the post-operative phase.

*Immediate Pre-operative Treatment.*—The patient should be under the influence of a basal narcotic from the early morning of the day of operation. Paraldehyde, given *per rectum*, in a dose of 1 fluid drachm (3.6 c.c.) per stone of body-weight, with a maximum of 8 drachms (28.8 c.c.), is generally effective and can be given without disturbance to the patient.  $1\frac{1}{2}$  to 3 gr.

(0.09 to 0.18 gm.) of pentobarbitone by the mouth the night before and again on the morning of operation may be substituted. Scopolamine-morphine "twilight-sleep" is equally effective,  $\frac{1}{4}$  gr. (16 mg.) morphine and  $\frac{1}{100}$  gr. (0.6 mg.) hyoscine hydrobromide being given subcutaneously two hours before operation and half quantities of each repeated one hour before going to the theatre. Bromethol per rectum, in half the anæsthetic dose, is also a useful drug. Each surgical service has its preference, and whichever method is adopted it is wise to master it thoroughly and to use it exclusively. Whatever the drug employed, the patient should be thoroughly drowsy on leaving the ward, and in well-managed cases may fall asleep before the anæsthetic is started. In no case should operation be attempted if the patient is acutely conscious and distressed or when the pulse-rate on the table rises to 130 or more. It is wiser to postpone the operation for a day or two than to risk a post-operative thyrotoxic crisis. For anæsthesia, nitrous oxide and oxygen is generally used, and is most satisfactory in skilled hands.

**Post-operative Treatment.**—The critical stormy period after thyroidectomy occurs in the first forty-eight hours after the operation. During this period the patient should be nursed in absolute quiet and seclusion, either in a room by herself or screened off in a corner of a general ward. Visitors and letters should be forbidden and medical examinations reduced to an absolute minimum. It is desirable that one day and one night nurse, specially trained or experienced in this work, should have charge of the patient. Their duties will include keeping an hourly record of pulse and temperature for the first twenty-four to thirty-six hours.

Owing to the high metabolism after the operation the temperature rises in most cases and few bedclothes are necessary or desirable. Heat loss is facilitated by cool air and light coverings and chills are very rare. Quiet is assured by hypodermic administration of morphia, which is repeated as required.

The administration of adequate amounts of fluids is most important, and, if the patient is dehydrated or unable to swallow, an intravenous drip transfusion of 6 per cent. glucose in saline should be started at once and continued till the patient is able to take fluids by the mouth. Glucose and orange drinks by mouth may then be substituted or used as adjuvants.

Iodine is frequently given post-operatively, potassium iodide being added to the intravenous infusion in doses of 5 to 10 gr. (0.3 to 0.6 gm.). If the patient has been thoroughly iodized before operation this is less necessary, but, once the patient is able to swallow, it is usual to continue iodine in the same dosage as in the pre-operative period for a week.

In many cases soreness of the throat is a troublesome post-operative feature. This is best controlled by steam inhalations, rest to the voice and sedatives. A watch must be kept for the occurrence of post-operative complications—crisis, tetany or hæmorrhage. These demand special treatment, to be considered below.

In an uncomplicated case such measures are sufficient to carry the patient over to the third or fourth day, when rapid improvement has as a rule been established. Further progress is uneventful, and slowing of the pulse, fall in temperature, subsidence of excitement and increase in general well-being indicate that the strict measures of isolation and sedative therapy can safely be relaxed. Transference to a medical ward may be allowed when the clips

or stitches are removed on the fourth or fifth day, and in many cases the patient is fit to get up for a short period some seven days after operation. Severe reaction, or the presence of cardiac failure, may delay progress considerably. Convalescence should be gradual and a holiday of one to two months enforced after discharge from hospital before a return to work is sanctioned.

**Post-operative Complications.**—*Hyperthyroid Crisis.*—This may occur post-operatively, or may supervene at any time in severe cases under medical treatment. A common precipitating factor is a pulmonary infection. In all cases its recognition is only too easy—the high fever, extreme tachycardia and great restlessness of the patient presenting an unforgettable clinical picture. The condition, once it has developed, is very intractable and is attended by a high death-rate. The essence of its treatment is in its *prevention*. It should very rarely occur after operation in cases properly treated pre-operatively and in which the time of operation has been well selected. Nor should it occur in well-supervised medical cases, for it is seldom that a case of moderate severity suddenly goes into crisis. It arises usually in those patients who have been deteriorating for some time, or who have run a severe course for months or years, and who therefore have not had timely and efficient treatment. It frequently occurs in cases of moderate or severe toxicity who have drifted out of medical supervision, and in the writer's experience has been more common in such "medical" cases than after thyroidectomy. It may also occur, with fatal results, after ill-timed operations for focal sepsis (tonsillectomy, etc.) in moderately toxic patients.

Established cases of hyperthyroid crisis should be treated on the lines detailed for the management of patients after thyroidectomy. Quiet and seclusion with adequate morphia are essentials. The promotion of heat loss and avoidance of hyperpyrexia can be aided by hydrotherapy. Tepid sponging may suffice or, in more desperate cases, cold packs and applications of ice-bags to the head and precordium may be required. Fluids must be administered per rectum and intravenously, a saline intravenous drip (2 to 4 pints) being probably the most efficient method. There is a danger of waterlogging and pulmonary oedema if large quantities of fluid are given *quickly* intravenously. The rate of administration by the drip method should not exceed one pint every sixty minutes. Iodine can be given, as 5 to 10 gr. (0.3 to 0.6 gm.) of potassium iodide in the intravenous saline. It is useless to employ thiouracil in hyperthyroid crisis owing to the number of days which must elapse before the drug produces its effect. Thus the patient would either have died or would have recovered before the action of thiouracil becomes manifest.

The efficient administration of oxygen (by B.L.B. mask, or by intranasal catheter, see p. 954) is an important part of the treatment and should be instituted early. Too often oxygen is administered only when the patient is already moribund. Digitalis does not control the tachycardia and is useless unless auricular fibrillation is present. Even then the drug appears less efficacious than in auricular fibrillation of other aetiology.

*Tetany.*—With modern surgical technique this complication is now very rare. Its treatment is dealt with on p. 435.

*Hæmorrhage.*—While the treatment of post-operative hæmorrhage must remain a surgical problem, it is necessary for the physician who may be

looking after a patient to recognize the indications for calling surgical aid. It is seldom that massive hæmorrhage occurs, with the symptoms of collapse, due to blood loss. Much more commonly hæmorrhage into the wound causes local tension and may bring about symptoms from pressure on the trachea. It should be remembered that oozing of serous fluid frequently occurs and may cause swelling in the region of the wound. In all cases of doubt as to the nature of such a swelling the opinion of the surgeon should be sought.

*Myxœdema.*—Cases of myxœdema arising after thyroidectomy must be treated with thyroid extract. The treatment does not differ from that in cases of myxœdema of other ætiology and should be along the lines suggested on p. 422.

*Radiation.*—Radiation by X-rays or radium has been used for many years in the treatment of hyperthyroidism. In this country it was widely employed some twenty to twenty-five years ago, and general dissatisfaction with its results and the striking success of surgical treatment led to an abandonment of its use. Before the introduction of thiouracil treatment radiation had again come to be more widely employed, and there could be no doubt that the modern technique used produced some degree of improvement in a considerable proportion of cases. X-ray treatment, therefore, had a place in the treatment of mild thyrotoxicosis in young people in whom thyroidectomy was undesirable, or in patients with primary thyrotoxicosis who refused operation or whose dread of it threatened a mental breakdown. The great success of thiouracil, however, in the treatment of such cases has made resort to such treatment superfluous, and in the writer's opinion it has entirely superseded radiation in thyrotoxicosis.

Recent reports from America claim striking beneficial effects in thyrotoxicosis from the administration of radio-active iodine. Whatever be the immediate benefits of such treatment—and there seems little reason to doubt them—radio-active compounds will have to be used with the greatest caution in human therapeutics; we know little of the ultimate results of such treatment, and, by its possible interference with the genes of the patient, it may even have effects on generations yet unborn, though it is true that radio-active iodine is a relatively short-lived isotope.

## THE PARATHYROID GLANDS

### TETANIA PARATHYROPRIVA

Clinically this condition may result from a parathyroidectomy undertaken for generalized fibrocystic osteitis or from a total or subtotal thyroidectomy. The symptoms, which may become manifest as early as twenty-four hours after the operation or may be delayed in their onset for a week, rapidly become serious and demand urgent treatment. If carpo-pedal spasm or laryngismus is already apparent when the patient is seen, an intravenous injection of calcium gluconate should immediately be given. Ten to twenty cubic centimetres of a 20 per cent. solution should be injected very slowly into one of the veins, five to eight minutes being allowed for the injection. Shortly afterwards a similar amount should be administered intramuscularly. The intravenous injection causes an almost immediate

disappearance of the symptoms of tetany while the intramuscular administration helps to prolong the effect. The whole procedure may be repeated if the symptoms reappear, which will probably be necessary as the total amount of calcium given in this way is exceedingly small.

It is wise, however, to begin parathyroid or vitamin D medication as soon as possible. Recent work has shown that the latter is the more efficient, and it is probable that the administration of parathyroid extract will be abandoned for this purpose because of its much greater cost and of the tendency for its effect to be diminished by long-continued use in any one patient. If there is an indication for parathyroid therapy it is at the onset of tetany when an intramuscular injection of 20 to 60 units, depending on the severity of the case, will produce a rise in serum calcium which begins within six hours and is maintained for about eighteen hours. The initial dose can be repeated every six hours provided a careful watch is kept on the level of the serum calcium, which should not exceed 13 mg. per cent. Tetany following removal of a parathyroid tumour does not generally last longer than two or three days, after which time the remaining parathyroid tissue is usually capable of producing a sufficiency of hormone. It is in this type of case that intramuscular injections of parathyroid may effectively tide over the period of hypocalcæmia until the endogenous secretion of hormone has reached a satisfactory level. When, however, the condition has resulted from thyroidectomy there may be little or no parathyroid tissue left in the body, in which case vitamin D therapy is much more satisfactory. Dihydratachysterol, a derivative of irradiated ergosterol and therefore closely allied to vitamin D, has the reputation of being much more effective than vitamin D, but when the latter substance is given in sufficient amount it is equally efficient. Dihydratachysterol should be given orally in daily doses of 3 c.c. of an oily solution containing 5 mg. per c.c. of basic substance until the serum calcium amounts to 9 mg. per cent. Thereafter daily doses of 0.5 to 1 mg. can be given. This dosage, however, should be controlled by a rough estimation of the amount of calcium being excreted in a twenty-four-hours' specimen of urine, which may be done very simply by the use of Sulcowicz's test.<sup>1</sup> If a marked turbidity appears in the urine on applying this test the dosage should be reduced. Vitamin D in doses of 1.0 to 2.0 mg. of calciferol (equivalent to 40,000-80,000 international units of vitamin D) has been shown to be equally effective in raising the serum calcium level, and in view of its greater availability should undoubtedly be used for maintaining a normal level of calcæmia. Occasionally it may be necessary to use much larger doses. In one instance daily doses of 500,000 units were given for fifty days, resulting in an increase of serum calcium and the disappearance of symptoms, the patient remaining well for at least three months without further treatment. Tablets of high-potency ostelin (Glaxo) have been specially designed to suit this scheme of dosage. Each tablet contains 50,000 international units of vitamin D or 1.25 mg. of pure crystalline calciferol. Intensive vitamin D therapy over a long period has been remarkably free from cases of severe intolerance

<sup>1</sup> Sulcowicz's Test.—The reagent is made as follows: 2.5 gm. of oxalic acid, 2.5 gm. of ammonium oxalate and 5 c.c. of glacial acetic acid are dissolved in distilled water and the volume made up to 150 c.c. To 5 c.c. of urine an equal amount of reagent is added. If there is no precipitate the serum calcium level is below the normal limits; if there is a fine white cloud a moderate amount of calcium is present in the urine and the level of serum calcium may be regarded as satisfactory, while a milky precipitate indicates hypercalcæmia.

when these pure preparations are used. Such cases do occur, however, and it is essential that patients be observed adequately during treatment and the urine tested regularly by the Sulcowicz test. This will give a much earlier warning of hypercalcaemia than the more elaborate and time-consuming determination of the serum calcium.

The diet must be rich in milk and milk products and it is advisable to give 120 gr. (7.2 gm.) of calcium gluconate or lactate by the mouth daily in divided doses.

**Idiopathic Hypoparathyroidism.**—This rare condition is treated on the same lines as those outlined for post-operative tetany.

### HYPERPARATHYROIDISM

The clinical picture designated as generalized fibro-cystic osteitis is the result of overaction of the parathyroid glands. It is characterized by pains in the limbs and fractures; occasionally attention is drawn to the condition by renal colic produced by calculi in the urinary tract, the formation of which frequently precedes generalized fibro-cystic osteitis. It is now, indeed, recognized that hyperparathyroidism is a more common aetiological factor in the formation of renal calculi than used to be supposed. X-ray examination reveals the presence of multiple cystic tumours of the bones, especially the long bones. Biochemical examination of the blood is of considerable importance in differentiating this disease from other pathological conditions of the bones such as focal osteitis fibrosa. In the generalized form the serum calcium is high, the serum phosphorus is low and the plasma phosphatase is greatly increased. These findings are important as indications of hypersecretion of the parathyroid hormone. Just as, however, the blood urea concentration is only raised in advanced cases of chronic nephritis and is normal in the early stages of the disease, so the changes in the blood only occur in advanced hyperparathyroidism when renal failure has occurred and the kidneys can no longer concentrate the excess calcium from the blood into the urine. Thus, a normal blood calcium does not necessarily exclude a diagnosis of renal stone due to hyperparathyroidism or of generalized fibro-cystic osteitis. Sulcowicz's test (see footnote, p. 436), when positive, will give an earlier indication of hyperparathyroidism than the blood chemistry. Should this indicate hypersecretion of the parathyroid hormone, an exploratory operation should be performed in the hope of removing a parathyroid adenoma. The simple clinical examination of the neck seldom reveals the presence of a tumour, and even at operation its detection may be exceedingly difficult.

Prior to operation, the patient's calcium stores should be replenished by the administration of a diet rich in milk and the giving of calcium salts (gluconate).

The post-operative treatment is carried out on general lines, but one must be on the lookout for early symptoms of tetany. In any case, abundant calcium should be given both in the diet (milk) and as calcium gluconate or other salt. If tetany makes its appearance it is necessary to begin the intensive therapy noted under post-operative tetany.

The results of surgical treatment of generalized osteitis fibro-cystica are good. Very soon the pains in the limbs disappear, and there is a great

improvement in health with disappearance of skeletal and urinary symptoms. Naturally it takes very much longer for the bones to recover their normal texture and months may elapse before there is much reduction of the plasma phosphatase. This emphasizes the necessity for continuing a high calcium diet with abundance of vitamin D.

## THE SUPRARENAL GLANDS

### ADDISON'S DISEASE

It has been definitely established that Addison's disease is the result of deficiency of the adrenal cortical hormone. The exact function of this hormone is still controversial, but there is no doubt that when it is lacking, sodium and water are excreted in excess from the blood into the urine while potassium is retained, and in addition some fundamental disturbance of carbohydrate metabolism occurs, resulting in a tendency to hypoglycæmia. In association with these changes in body chemistry, concentration of the blood occurs with a diminution in plasma volume. The changes which concern sodium, potassium and diminished blood volume are so interdependent that it is difficult to determine which of them is initially responsible for the syndrome, but treatment should aim at redressing all these disturbances of function. The loss of sodium and the dehydration are made good by supplying an abundance of sodium chloride and water; an excessive intake of potassium salts is avoided so as not to exacerbate the tendency to increased retention of that element; a plentiful supply of carbohydrate is provided to combat the hypoglycæmia; but the principal therapeutic weapon in Addison's disease is to replace the deficient cortical hormone either by the use of the natural preparation itself or more often of its synthetic analogue.

Before the introduction of modern therapeutic measures the disease progressed inexorably to a fatal issue in periods of time varying from a few months to not much more than two years. Since the introduction of potent substitution therapy the prognosis has greatly improved, though the life of a patient with Addison's disease is still precarious owing to the liability of Addisonian crisis, which may be precipitated by intercurrent infections, sometimes of a trivial nature, or by the administration of drugs such as morphine or anæsthetics to which patients with Addison's disease are notoriously intolerant. Such crises, which usually occur very suddenly, are characterized by a high temperature, intractable vomiting, delirium, severe dehydration and shock. In managing a case of Addison's disease the practitioner should seek to prevent crises by increasing substitution therapy on the first sign of an intercurrent infection, and by avoiding the use of general anæsthetics, particularly chloroform and ether, the opiates and potassium salts.

**Treatment in Crisis.**—In Addisonian crisis treatment consists in the administration of large doses of cortical extract and in combating shock, dehydration, hypoglycæmia and sodium depletion by warmth and the administration by intravenous-drip transfusion of 5 per cent. glucose solution in saline. This should not be given more rapidly than one pint every two hours. In all, from three to six pints may be necessary.

During crisis, cortical extract should be given in preference to the syn-

thetic preparation, partly because it is a more complete substitution therapy and partly because it is a watery extract and can be given intravenously. Cortical extract is sold commercially as Cortin (Organon), 1 c.c.=50 gm. of whole gland; Eschatin (P. D. & Co.), 1 c.c.=40 gm. cortex; and Eucortone (Allen & Hanbury), 1 c.c.=75 gm. cortex. Initially 20 to 30 c.c. of one or other of these preparations should be given intravenously. During crisis, patients commonly react with a sharp febrile attack or rigor to this parenteral treatment, which should not, however, deter the physician from repeating the intravenous dose in four hours in critically ill patients. Thereafter the hormone can usually be given intramuscularly in 5 to 10 c.c. doses every six hours, the frequency of the dose being gradually reduced as the crisis subsides. The above is, of course, merely a rough indication of an average course of treatment. Just as in diabetic coma there is no "dose" of insulin, so in Addisonian crisis there is no "dose" of cortical extract. Each case has to be treated as an individual problem. Unfortunately the treatment is very expensive, since 10 c.c. of cortical extract costs about thirty shillings.

**Maintenance Treatment.**—Since corticosterone was isolated in 1937 it has proved possible to synthesize a closely allied compound—desoxycorticosterone acetate (D.O.C.A.)—which possesses the essential biological properties of corticosterone. Of all the compounds isolated from the adrenal cortex, D.O.C.A. has the greatest effect in conserving sodium chloride and water and in causing excretion of potassium. It has little demonstrable effect in maintaining normal carbohydrate metabolism. Since it does not provide a complete substitution therapy for natural adrenal cortex it is, as we have seen, better to adhere to cortical extracts for the rescue of patients during crises, especially as D.O.C.A., being an oily solution, cannot be given intravenously. Nevertheless, owing to its much lower cost, smaller bulk and stronger effect in conserving sodium, D.O.C.A. is the drug of choice for maintenance treatment.

D.O.C.A. is inactive when swallowed, and its administration sublingually as tablets or dissolved in propylene glycol, although effective, is wasteful and very costly. It can be given intramuscularly dissolved in sesame oil, 1 c.c. containing 5 mg. of the drug, approximately equal to 10 c.c. of cortical extract. A patient who is in bad condition may require as much as 5 mg. a day; a mild or well-stabilized case may be maintained by as little as 5 mg. once or twice a week. Dosage must be regulated by the patient's general condition and subjective symptoms, by the blood pressure, the blood chemistry and, particularly, by the weight, which is the most reliable single index of progress. A word of warning is necessary in using blood chemistry as a reliable yardstick for the control of treatment. It is true that in Addisonian crisis or approaching crisis there is a greatly increased excretion of sodium and chloride with a fall in their serum values and a corresponding rise in the serum potassium, inorganic phosphate and urea concentrations, while the blood sugar concentration tends to be low. It is only when the patient is severely ill, however, that these changes are appreciable and in the ordinary case blood chemistry estimations do not provide a very delicate diagnostic or prognostic index.

When a patient with Addison's disease is encountered for the first time, injections of D.O.C.A. should be started straight away, and after a maximal improvement has been achieved by this means implantation therapy should be undertaken.



Implantation of D.O.C.A. is the most economical, effective and least troublesome method of administering the drug. 400 mg. in the form of pellets—each containing 100 mg.—are inserted into the deep subcutaneous tissues of the abdomen through a small incision which can be closed by a couple of stitches. There is a tendency for such pellets to be extruded in the course of time if they are implanted too superficially or if the edges of the little wound are not carefully undermined and the pellets tucked into pockets well away from the line of the incision. If these precautions are undertaken, not more than 10 per cent. of the pellets should be lost in this way. The effect of D.O.C.A. thus implanted can be maintained for periods of time varying from six months to a year without the necessity of frequent oily intramuscular injections unless an intercurrent infection should temporarily necessitate the potentiation of the implant, when appropriate intramuscular injections of the drug should at once be given. Several factors influence the absorption rate from the implant, such as the surface area and density of the pellets, the vascularity of the implantation site and the tissue reaction to a foreign substance. There is no reason to suppose that the body will absorb just the right amount of hormone needed for its normal function, and, though inadequate absorption may be made good by occasional injections, excessive absorption—giving rise to serious hypertension and massive oedema if much salt is given coincidentally—can only be remedied by the surgical removal of the implant. On theoretical grounds, therefore, it would seem somewhat unjustifiable to implant potent crystalline hormones in large amounts and to trust to nature to regulate wisely their subsequent absorption. Nevertheless, the writer has to record the most satisfactory results in a considerable number of patients treated by this method for some years. They have remained in good health and shown no serious toxic manifestations apart from a transient moderate hypertension in a few cases during the period of maximum absorption from the implant. Such hypertension has been associated with a feeling of particular well-being on the part of those patients in whom it has been observed. An appraisalment of the patient's subjective symptoms, his blood pressure, blood chemistry and weight should indicate when a further implantation is becoming necessary. Should doubt arise as to the activity of the implant, the giving of 15 gm. of sodium salt a day is often a useful test. If the implant is still active this will invariably result in some oedema of his face and ankles making its appearance within a fortnight. If this does not occur the implant has almost certainly become used up or has become so walled off by fibrous tissue as to be rendered inactive.

Until the potent action of D.O.C.A. in causing retention of sodium was recognized, the basis of maintenance treatment consisted in the administration of sodium salts. An ample supply of this element lessens the requirement of D.O.C.A. or cortical extract, and indeed it is sometimes possible to maintain health in mild cases by the use of sodium salts alone. Patients with Addison's disease are much more tolerant to sodium chloride than healthy subjects and can often take doses up to 15 gm. a day in addition to their ordinary intake without nausea being induced. Since the deficiency of sodium is more important than the deficiency of chloride, sodium citrate or bicarbonate may be used to replace some of the sodium chloride. A suitable method consists in the administration during the day of half a pint of water containing, as a maximum, 5 gm. of sodium chloride and  $2\frac{1}{2}$  gm.

of sodium citrate or bicarbonate suitably flavoured. D.O.C.A. has such powerful effects in causing retention of sodium that serious generalized anasarca easily results when large doses of D.O.C.A. and sodium salts are given simultaneously. When, therefore, D.O.C.A. is used rather than cortical extract, the total additional daily dose of sodium salt should not exceed  $7\frac{1}{2}$  gm., and this should be omitted on the first sign of œdema. Indeed, some authorities now believe that salt, additional to that taken with food, should not be prescribed with D.O.C.A., though the writer believes this to be too extreme a view.

With the object of preventing an excessively high concentration of potassium in the blood, diets with a very low potassium content used to be prescribed. Such diets were unpleasant and irksome, and now that potent substitution therapy is practicable, this meticulous complication of treatment has become superfluous, provided the mineral in the form of medicine, such as potassium citrate or potassium iodide, is excluded.

Fully 50 per cent. of cases of Addison's disease are due to tuberculosis, and active tuberculous disease in other parts of the body, particularly in the lungs, bones and genito-urinary tract, must not be overlooked and when present must receive appropriate treatment.

#### ADRENAL APOPLEXY

(*Friderichsen-Waterhouse Syndrome*)

In the course of fulminating purpuras and septicæmias—particularly acute meningococcal septicæmia—hæmorrhage may occur into the adrenals. The resulting disease, characterized by shock, abdominal pain, intense purple cyanosis, ecchymotic hæmorrhages and a collapsed blood pressure, presents an unforgettable clinical picture. The patient speedily relapses into unconsciousness and a fatal issue is the rule, sometimes within a few hours.

Occasionally the adrenal apoplexy is not massive and energetic treatment may save life. Apart from the treatment of the associated septicæmia with sulphonamides and penicillin the treatment is the same as for severe Addisonian crisis, with large intravenous doses of cortical extract and an intravenous-drip transfusion of 5 per cent. glucose in saline.

#### TUMOURS OF THE ADRENALS

**Tumours of the Adrenal Cortex.**—Hyperfunction of the adrenal cortex is usually due to cortical adenomata or carcinomata and may give rise to the following syndromes according to the age at which the over-activity occurs: (1) in embryonic life to pseudo-hermaphrodisim; (2) before puberty to sexual precocity with coincident masculine change in the female; (3) at or after puberty to virilism (the adreno-genital syndrome).

In *pseudo-hermaphrodisim* little can be done to improve the condition though the prognosis as to life is good.

When *sexual precocity* is due to a cortical tumour the prognosis is bad owing to the frequency of a malignant ætiology, but an attempt should be made to remove the responsible tumour.

In the *adreno-genital syndrome*, which may be indistinguishable from Cushing's syndrome, a striking clinical reversion to normal may follow the

removal of a cortical adenoma or a suprarenal gland with cortical hyperplasia, particularly if the syndrome has not persisted for many years. It may be difficult to know which adrenal is involved and both may have to be explored. An excretion pyelography may occasionally show the growth to be distorting one of the renal pelves, or the tumour may sometimes be delineated radiologically after injecting air into the peri-renal space—a somewhat delicate specialist procedure. Acute adrenal insufficiency may follow adrenalectomy since the remaining gland may be partially atrophied. D.O.C.A. or cortin should therefore be given for some days before and after operation.

**Tumours of the Adrenal Medulla.**—*Neuroblastomata of the adrenal medulla* are extremely malignant tumours which are practically never diagnosed in time to permit of their successful removal.

Hyperfunctioning tumours of the adrenal medulla of *chromophile* tissue result in the rare condition of paroxysmal hypertension. Such tumours are adenomatous and usually benign. They probably produce their effects by discharging pathological quantities of adrenaline into the blood. The condition eventually results in degenerative changes in the arterioles and in ischæmic kidneys with permanent hypertension.

The clinical picture is so striking that diagnosis is easy during the paroxysmal stage, when the removal of the adenoma is likely to cure the condition. The difficulties of diagnosing which adrenal is involved and the dangers attending adrenalectomy are the same as in the adreno-genital syndrome (*vide supra*).

## THE PITUITARY GLAND

### DIABETES INSIPIDUS

Diabetes insipidus, characterized by marked polyuria and thirst, is generally attributed to a lesion in the floor of the third ventricle anterior to the tuber cinereum or to one in the anterior hypothalamus, an extension of which forms the posterior part of the pituitary. The nature of the lesion varies in different patients and may be the result of syphilis, neoplasm, trauma or encephalitis, while there is a group of patients in whom there appears to be a hereditary or familial tendency.

If there is evidence of syphilis, vigorous anti-luetic treatment should be instituted. A neoplasm causing this lesion is at present almost always inaccessible to surgical treatment, although deep X-ray therapy has been said to yield promising results. In most cases treatment should be directed to the relief of the thirst and polyuria. For this purpose intramuscular injections of posterior pituitary extract or preferably a suspension of the pressor fraction (pitressin tannate, Parke, Davis & Co.) are of value. Care must be taken to shake the suspension thoroughly before it is injected intramuscularly. Dosage varies from case to case and at different times in the same patient. An average dose will consist of 0.5 c.c. of pitressin tannate injected just before bedtime, and this may be reduced or increased as the results demand. The patient's ability to lead a normal life during both the day and night is the test for satisfactory control.

It is worth noting that most of the unpleasant reactions such as intestinal colic, nausea and vomiting which may occur after soluble pitressin do not

appear to follow injections of the tannate. With the small dose which is here recommended it is very unlikely that the retention of water will be excessive.

The posterior pituitary hormone probably increases tubular reabsorption in the kidney. This leads to an increase in the specific gravity of the urine and marked diminution in urinary volume with consequent retention of water in the tissues and alleviation of thirst. A fluid intake and output almost within normal limits is generally achieved within a few days of the start of pitressin medication.

### ADENOMATA OF THE PITUITARY

Adenomata of the pituitary body are restricted to the anterior lobe and may be classified as (a) chromophobe or agranulocytic, (b) eosinophil, and (c) basophil, according to the staining reactions of the cells composing the tumour. The symptoms and signs produced depend upon the pressure exerted on the remaining tissue of the anterior lobe and the surrounding structures, upon the extent of actual destruction and the nature of the secretion produced by the tumour cells.

**The Chromophobe Adenoma.**—A tumour of the chromophobe cells, to which no secretory function has yet been attributed, manifests itself by the effects of pressure on and destruction of pituitary tissue and such structures as the optic chiasma and hypothalamus. The only treatment which holds out any hope is surgical removal, since the chromophobe cells do not appear to be sensitive to X-rays. Increasing loss of eyesight is an important indication for surgical interference, which should be attempted as soon as possible before the destruction of tissue is advanced. Signs of pituitary cachexia (Simmond's disease) not infrequently follow the removal of such tumours, the treatment of which is discussed on p. 444.

**The Acidophil or Eosinophil Adenoma.**—This gives rise to the clinical conditions of gigantism or acromegaly according to the age of the patient. In addition, signs of pressure on the optic paths are generally present. Deep X-ray therapy is frequently successful in arresting the growth of this type of tumour and should always be tried before resorting to surgical treatment, except in those cases showing a very rapid contraction of the visual fields. It is not unusual to encounter abortive or "burnt out" cases of acromegaly. These require no treatment unless signs of pituitary cachexia are present.

**The Basophil Adenoma.**—This produces the clinical manifestations generally known by the term "Cushing's syndrome." It is extremely doubtful, however, whether the primary lesion is situated in the pituitary in such cases. Modern opinion tends to the belief that Cushing's syndrome is due to an adenoma or hyperplasia of the adrenal cortex rather than to the changes which are also present in the basophil cells of the pituitary. It is impracticable to remove surgically the tiny tumour which may be present, and X-ray therapy to the pituitary region gives very disappointing results in basophil as opposed to eosinophil adenomata. The prolonged use of testosterone propionate by intramuscular injection three times a week in doses of 25 mg. has been recommended. The writer has not been impressed by the results of such treatment. The removal of a hypertrophied or adenomatous adrenal gland is likely to be a more hopeful therapeutic

approach. Owing to the associated osteoporosis, orthopædic supports for the spine are often necessary.

### PITUITARY INFANTILISM

Pituitary infantilism, which generally becomes manifest before the tenth year of life, is associated with defective production of the growth hormones and is frequently associated with a failure of the gonadotrophic secretions. The clinical picture is one of dwarfism with defective development of the primary and secondary sex characters. The mental processes, although sometimes unaffected, generally remain childish.

At present there is no anterior pituitary growth hormone on the market which seems to be effective. In addition the thyrotropic hormone, which is present in excess in growing animals, is not available for therapeutic use. An attempt should be made to stimulate the development of the sex hormones by the intramuscular injection of serum gonadotropic hormones (see pp. 448, 967). This treatment should be withheld till the age of fifteen or sixteen, as the administration of such extracts may lead to closure of the epiphyses before a sufficient degree of growth has been obtained. Interrupted courses of 500 units should be given twice a week for six weeks, with an interval of three months between the courses.

### PITUITARY CACHEXIA

*(Simmond's Disease)*

Pituitary cachexia, characterized by marked wasting, particularly of the muscles, premature senility and failure of sexual function, results from destruction of the anterior lobe of the pituitary with consequent deficiency of its hormones. The causal factor may be tumour, syphilis, tuberculosis, cystic degeneration, thrombosis or embolism. The latter has been observed following the termination of pregnancy. So-called anorexia nervosa results in pituitary cachexia with similar clinical manifestations. In this condition the ætiological factor is some psychological shock or strain which inhibits anterior pituitary function. In early or mild cases the process may be reversible.

A satisfactory replacement of the defective anterior pituitary hormones is not possible and replacement therapy must be conducted at a lower level. Steroids which control salt, water and nitrogen metabolism may sometimes produce dramatic improvement, and of these testosterone propionate is the drug of choice. It can be administered most economically by the implantation of 600 mg., the process being repeated if necessary every three or four months. The technique for implantation is the same as that used for D.O.C.A. (see p. 440). In very severe cases 25 mg. of the drug can be given daily by intramuscular injection till improvement occurs, after which the interval between the injections can be gradually lengthened or an implant made. Thyroid therapy should be withheld till the metabolic balance is re-established by the use of testosterone. A high intake of protein is also very desirable, but may be impossible owing to the anorexia which is such a characteristic feature of the condition. The anorexia, however, often improves under the influence of testosterone therapy so as to permit of a gradually increasing intake of protein food.

## MALE HORMONE

Much has been written about the use of the male hormone, testosterone and its synthetic derivatives, but it must be confessed that their value in therapeutics has not yet been clearly established.

The two functions of the testes, the production of spermatozoa and the secretion of the male hormone, are regulated by the gonadotrophic hormones secreted by the anterior lobe of the pituitary. As far as spermatogenesis is concerned there is no method at present available for initiating or restoring the power to produce spermatozoa, and the therapeutic functions of the male hormone are limited to the remedy of any defects produced by absence or deficiency of the internal secretion of the testes. It is therefore of importance to appreciate the effects of testicular insufficiency. These vary according as to whether the insufficiency commences before or after the onset of puberty. In the former case a state of eunuchoidism is produced, characterized by excessive length of the limbs, poor muscular development, high-pitched voice, female type of thyroid cartilage and lack of facial and pubic hair. When testicular insufficiency occurs after puberty there is no skeletal abnormality, but there may be excessive deposit of adipose tissue in the mammary, trochanteric and pubic regions. The skin is soft and dry with soft hair of the feminine type, the complexion is sallow and there may be flushings suggestive of those occurring at the menopause. Sexual functions are greatly diminished or absent, while there is generally decrease in the size of the external genitalia, especially penis and scrotum. Psychological abnormalities are described, but it is uncertain whether these are due directly to lack of testicular hormone, to deterioration of the intellect resulting from premature senility or to the mental disturbance associated with the consciousness of impotence.

The chief indication for male hormone therapy is *eunuchoidism*, whether due to defective development or to castration. It is well, however, to remember that many boys mature late, so that it is foolish psychologically, and may actually be harmful, to commence the administration of androgens too early, since it may lead to premature cessation of growth. The best method is to inject 25 mg. of testosterone propionate in oil daily until signs of improvement are noted. Thereafter the dose should be reduced until a maintenance dose, usually about 25 mg. weekly, is found which gives the best results. Subcutaneous implantation of pellets to a total of 600 mg. (for technique see p. 440) is much the most economical and satisfactory method of treatment. Such an implant remains active for at least three months. Oral administration is expensive and uncertain in clinical effect since androgens are apparently inactivated in the liver: for this route methyl testosterone is recommended in doses up to 150 mg. daily. It is probable that sublingual administration may prove more efficacious. In the patient who responds to treatment, changes are noted within a few weeks. The genitalia, with the exception of the testes, become larger, while the character of the skin, hair and voice approximate to those found in the normal male. Spermatogenesis is not affected, but there is sometimes a return of sexual desire.

Though testosterone therapy may bring about considerable development in the external genitalia of eunuchs and may even stimulate in them libido

and potentia, it must be emphasized that it has no such effects in adult males who do not show evidence of endocrine disorder. In the writer's opinion the practice of prescribing testosterone as treatment for male sterility and sometimes even as an aphrodisiac is justifiable on no sound clinical evidence nor on any theoretical consideration. A great deal of male sterility is, of course, psychological in origin and the injection of male hormone may act as a psychological stimulus; in small doses it may do no harm except to the patient's pocket, but in large doses it will inhibit spermatogenesis. Recent studies in male sterility by means of testicular biopsies have divided the organic cases into two classes: the first exhibits degeneration in the seminiferous tubules with surrounding fibrosis, thought to be due to infection or to a nutritional defect; the second exhibits tubular impairment without fibrosis, which is assumed to indicate pituitary gonadotrophic deficiency. The most rational treatment for this latter class is the injection of gonadotrophic hormones, but unequivocal success is rare. Treatment by testosterone is certainly irrational, because actual experiment has shown that it produces shrunken germinal cells in the seminiferous tubules.

Among other indications for androgen therapy may be mentioned *Undescended Testes* and *Premature Senility*. It is extremely doubtful, however, whether any good effect can really be attributed to their treatment with androgen. The literature is not convincing, and in the present state of knowledge it seems unwise to use the androgens as a routine therapeutic measure for these conditions. Some workers have recommended the administration of testosterone to the female for the treatment of metropathia (see p. 451).

The male hormone will probably be found to be of more general value for its metabolic effect in conserving nitrogen than for its androgenic action in eunuchoidism, which, though striking, has a relatively small application. Even its beneficial effect on eunuchs is to some extent due to the improvement in their musculature consequent on its anabolic action on nitrogen metabolism. Thus it may be used not only in pituitary cachexia (see p. 444) but to assist in the correction of other conditions associated with a severely negative nitrogen balance, particularly in the preparation of cachectic patients for surgery. The claims which have been made for testosterone in the treatment of enuresis, prostatic hypertrophy and angina of effort have often been exaggerated, and any benefit which results from such therapy is almost certainly due to the improvement which it brings about in the muscle tone of the bladder and heart and not to its androgenic action.

D. M. DUNLOP.

## FEMALE SEX ENDOCRINOLOGY

### INTRODUCTION

The intelligent treatment of menstrual and reproductive abnormalities requires not only some knowledge of the physiological processes involved in normal menstrual function but also an understanding of the actions of the various hormone preparations which are available for clinical use. The following is a brief epitome of the cyclical changes which occur in the ovaries and uterine endometrium during a normal cycle.

1. The activity of the ovaries is regulated by the gonadotrophic hormone or hormones of the anterior pituitary. There is a difference of opinion as to whether there is one gonadotrophic hormone which, in varying concentration, promotes the complete cycle in the ovary, or whether there are two gonadotrophic hormones, one stimulating the development of Graafian follicles and ovulation—the so-called follicle-stimulating hormone, and the other promoting the development of the corpus luteum—the luteinizing or interstitial cell stimulating hormone.

2. The ovaries, stimulated by the anterior pituitary, give rise to several Graafian follicles which during their development elaborate a specific hormone, oestradiol. This hormone, in its turn, has a stimulating effect on the uterine endometrium inducing the pre-ovulatory or proliferative phase.

3. One follicle in each cycle reaches full development and ruptures, usually about the 13th or 14th day of the cycle counting the first day of menstruation as day one, releasing an ovum. The ruptured follicle, still under the primary pituitary stimulus, becomes luteinized and a corpus luteum is formed. The corpus luteum also elaborates a specific hormone—progesterone, but in addition secretes oestradiol. Progesterone changes the character and structure of the uterine endometrium into the so-called secretory, post-ovulatory or pre-menstrual phase.

4. If fertilization fails to occur the endometrium at the end of the secretory phase breaks down and menstruation follows.

Although there are many hypotheses, the actual cause of the bleeding itself is not yet explained.

It is difficult to estimate the importance of the rôle played by certain of the other endocrine glands, such as the thyroid, adrenals and pancreas, in menstrual and reproductive function. All are essential to a general hormonal balance, and there is evidence to suggest that dysfunction of any one of these glands may adversely affect the menstrual and reproductive process. Chief interest, however, has been centred around those glands vitally concerned in the menstrual function, namely, the pituitary and ovaries.

### GONADOTROPHIC HORMONES

It has been conclusively demonstrated that anterior pituitary gland extracts are effective in stimulating gonadal function in the hypophysectomized experimental animal. Such extracts would be of very great value in the treatment of patients exhibiting ovarian hypofunction. Potent extracts, however, are not only very difficult to prepare, but they are so unstable that they readily lose their potency. At the present time there are no reliable *anterior pituitary gland* extracts available for clinical use. There are, however, two preparations which, though not truly hypophyseal in character, have an anterior pituitary-like action. From the point of view of their therapeutic application, it is most important that the biological effect of these two substances should be clearly understood.

The substances are:—

1. Urine or chorionic gonadotrophic hormone.
2. Serum or equine gonadotrophic hormone.

**Urine Gonadotrophic Hormone.**—This hormone is present in the urine in large amounts during pregnancy and is the basis of the Aschheim-Zondek test for pregnancy. It is also excreted in the urine in cases of chorion



epithelioma and certain embryonic testicular tumours. Thus it is extra-hypophyseal in origin and the available evidence indicates that it is elaborated by chorionic tissue. The predominant effect of this autocoid on the ovaries of immature animals is luteinization. The administration of this hormone does *not* stimulate the development of Graafian follicles in humans, but it may produce luteinization in follicles already formed. The indications, therefore, for its clinical use are very limited.

**Serum Gonadotrophic Hormone.**—This hormone is found in the blood serum of pregnant mares during the middle third of their pregnancy. It simulates chorionic gonadotrophic hormone in that it *does* stimulate the growth of primordial follicles. In the latter respect serum gonadotrophic hormone closely resembles the action of anterior pituitary gland extracts and thus it is a useful therapeutic agent. Experimentally and clinically it has been found that the effect of this preparation can be enhanced by the simultaneous administration of chorionic gonadotrophic hormone.

**Standardization of the Gonadotrophic Hormones.**—Methods of standardization are based on the minimum amount of the hormone required to induce ovarian changes in immature rats or mice. The establishment of a unit in terms of an international standard has clarified the previous difficulty in regard to dosage. According to the standard preparation from human pregnancy urine 1 unit=0.1 mg., and the standard preparation from the serum of pregnant mares 1 unit=0.25 mg.

**Methods of Administration of Gonadotrophic Hormones.**—Anterior pituitary and anterior pituitary-like preparations are not effective when given orally. These preparations should be given by the intramuscular or intravenous route. When a powder preparation is used the powder should be carefully dissolved in the solvent and the site of injection thoroughly massaged. This precaution avoids or minimizes any local or general reaction to the injection. Intravenous administration should be preceded by a skin sensitivity test in order to avoid unfavourable reactions. Anterior pituitary and anterior pituitary-like preparations retain their optimum potency when kept in a refrigerator.

For preparations see Appendix, p. 967.

## OVARIAN HORMONES

Two hormones are secreted by the ovaries: (a) œstradiol, œstrogen or œstrogenic hormone, and (b) progesterone or corpus luteum hormone.

**œstradiol or œstrogenic Hormone.**—An œstrogenic substance is one which, when injected into the ovariectomized animal such as the rodent, induces the changes in the reproductive tract characteristic of true œstrus. During œstrus the vaginal epithelium shows cornification and this can readily be demonstrated by the vaginal smear test. Only leucocytes are found in the vaginal smear during dioestrus or the resting phase.

œstrogenic hormone is present in the blood and urine of normal men and women. A very high concentration of the hormone is found in the blood and urine of pregnant women.

Substances with œstrogenic activity have been found widely distributed in the plant and animal kingdom. In the human female three important compounds, each a phenanthrene derivative, have been isolated and purified, *viz.*, œstrone, œstriol and œstradiol. The most powerful of these three

compounds is œstradiol, and as it has been recovered from the follicular fluid of the ovary it is believed to be the naturally occurring œstrogenic principle—the female sex hormone.

The natural œstrogens have only a short period of action as they are very readily excreted in the urine. This may be overcome, however, by the administration of compounds from which the œstrogens are slowly liberated in the body. The most important of these compounds are the esters, and as such the œstrogens are used in clinical practice.

*Synthetic Œstrogenic Substances.*—The identification of the chemical structure of the natural œstrogens has stimulated efforts to synthesize them, but so far with no success. As a result of the research of Dodds and his co-workers, however, several compounds have been isolated which have a high œstrogenic activity. The two principal compounds first synthesized—derivatives of stilbene—were diethyl stilbœstrol or stilbœstrol, and dihydrostilbœstrol or hexœstrol. Both these substances are very active when given orally, whereas the natural œstrogens are relatively inactive when given by this route. These two synthetic compounds have been tested clinically and experimentally and have been found to simulate all the known functions of the naturally occurring œstrogens. Their high activity by oral administration is of considerable clinical importance, the only disadvantage being that they have a tendency to cause nausea and vomiting in some cases. Several other œstrogenic substances such as dienœstrol, diphenyl bromoethylene, dehydrodoisynolic acid, triphenylchloroethylene, have been prepared synthetically. Clinical experience with these preparations justifies the assumption that they are less toxic than the compounds originally synthesized but they may not have the same œstrogenic activity.

*Physiological Actions of the Œstrogenic Hormone.*—1. The injection of œstrogenic hormone, natural or synthetic, stimulates œstrus in the castrated or immature experimental animal.

2. The œstrogens control the development of the secondary sexual characteristics and promote the growth of the reproductive tract in the female.

3. They induce the proliferative or pre-ovulatory change in the uterine endometrium, sensitize the uterine musculature, and stimulate capillary vaso-dilatation in the uterus.

4. Growth of the vaginal epithelium is stimulated by œstrogen and glycogen is deposited in the epithelial cells.

5. The anterior pituitary gonadotrophic hormone is inhibited by the œstrogens when given in sufficient concentration.

6. The development of the duct system of the breasts is most probably promoted by the œstrogenic hormone.

For Preparations see Appendix, p. 968.

**Progesterone or Corpus Luteum Hormone.**—The functionally active corpus luteum secretes œstrogenic hormone in addition to its specific hormone, progesterone. The latter is essential only for reproductive function. Progesterone does not reproduce its characteristic effect on the uterine endometrium without the prior action of œstrogenic hormone.

Several biologically inactive substances which are metabolic or breakdown products of progesterone—the most important of which is pregnanediol—are excreted in small amounts during the second half of the normal menstrual cycle and in large amounts during pregnancy. The

chemical estimation of pregnanediol in the urine is proving a fairly reliable index of corpus luteum activity.

*Physiological Actions of Progesterone.*—1. It promotes the secretory or pre-menstrual phase of the uterine endometrium previously sensitized by oestrogenic hormone.

2. Progesterone prepares the endometrium for the implantation of the fertilized ovum in that it induces the decidual reaction in the uterine endometrium, desensitizes the uterine musculature and thus maintains pregnancy in the very early stages.

3. The development of the alveolar systems of the breast is probably under the control of progesterone.

4. Progesterone is synergistic with oestrogenic hormone at certain concentrations but can be antagonistic when the oestrogen reaches a high blood concentration. Administration of progesterone in such circumstances causes elimination of the excess of oestrogen by urinary excretion.

For Preparations see Appendix, p. 969.

**Standardisation of Ovarian Hormones.**—The fixing of an international unit standard in the dosage of oestrogenic hormones brought order out of chaos but resulted in the dosage being frequently expressed in astronomical figures. The problem has been simplified by expressing the dosage as the actual weight of the hormone in milligrams. One milligram of pure oestrone contains 10,000 international units.

The international unit of progesterone is defined as the progestational activity present in 1 milligram of crystalline corpus luteum hormone. Therapeutically the dosage is expressed in milligrams.

**Methods of Administration of the Ovarian Hormones.**—The oestrogens may be given by inunction in the form of an ointment, vaginally as pessaries, orally or by intramuscular injection and by sub-fascial pellet implantation.

The choice of route of administration largely depends on the condition for which the hormone is given. As a general rule oral administration of synthetic oestrogen and intramuscular injection of natural oestrogen are effective for the majority of conditions for which they are indicated.

Progesterone is given orally and intramuscularly, but the effective oral concentration must be six times that given by injection. It may be given by sub-fascial pellet implantation in cases such as recurrent abortion where a prolonged and continuous absorption is desired.

## DISORDERS OF MENSTRUAL FUNCTION

**Functional Uterine Bleeding.**—Probably the most common cause of functional uterine bleeding is metropathia hæmorrhagica. This condition is characterized pathologically by cystic degeneration of Graafian follicles with absence of recent or active corpora lutea in the ovaries. There is hyperplasia of the uterine muscle with marked hyperplasia of the endometrium and cystic dilatation of the endometrial glands. The predominant symptom of the condition is irregular or prolonged uterine bleeding, frequently preceded by a period of amenorrhœa of six to ten weeks' duration. It is more common at puberty and the menopause, but may occur at any time during the period of reproductive life. The clinical and pathological manifestations of the condition are due, undoubtedly, to a dysfunction of the ovaries. It is not clear whether the ovarian dysfunction is due to some

change in the structure or reactivity of the ovaries, or if it is associated primarily with an abnormal functioning of the anterior pituitary. Both factors may be present in any one case.

The management of a case of metropathia hæmorrhagica requires the consideration of several specified lines of therapy: (a) general measures, (b) hormone therapy, (c) irradiation, (d) surgical treatment.

*General Measures.*—It is important that attention should be directed towards an improvement in general health. Nutritional faults should be corrected. Mild degrees of anæmia should be treated by the administration of iron and severe degrees by blood transfusion. Adequate rest, careful regulation of the bowel and avoidance of undue strain and anxiety are essential, especially at puberty.

*Hormone Therapy.*—This is particularly indicated in the younger woman, and in such cases it is, as a rule, successful. Its employment in women towards the end of the period of reproductive life should always be preceded by a very thorough pelvic examination and curettage of the uterus in order to exclude malignant disease. Hormones available for the treatment of metropathia hæmorrhagica are (a) progesterone, (b) testosterone and (c) thyroid.

Progesterone is given intramuscularly in doses of 10 to 20 mg. daily or 60 mg. orally for four to five days, starting at the onset of the bleeding. This dosage is usually effective in controlling the bleeding, but in some cases may have to be continued for a longer period. After the bleeding is controlled it is advisable to continue with progesterone therapy during the second half of the cycle over a period of three months, giving 10 to 20 mg. every third day for three injections, or the equivalent amount by oral administration.

Testosterone (male hormone) is also effective in metropathia hæmorrhagica. This preparation should be used with caution as it is sometimes associated with unpleasant effects such as hirsutism and change of voice, which may be minimized by limiting the total dosage during a menstrual cycle to 250 mg. The dose recommended is 25 mg. intramuscularly twice weekly for two weeks, followed by 10 mg. twice weekly for the next two weeks. Several courses of this treatment may be required before the condition is brought under control. Occasionally a period of amenorrhœa, varying in duration from two to three months, may be produced as a result of this therapy, after which there is a return of the normal cycle.

Thyroid extract 1 gr. (0.06 gm.) once or twice daily is occasionally efficacious, especially in young girls, when the menstrual abnormality is associated with signs of hypothyroidism.

*Irradiation.*—The induction of an artificial menopause with radium or X-irradiation of the ovaries is an effective therapeutic measure for menopausal patients. Its employment in younger individuals with the object of inducing temporary amenorrhœa is, however, fraught with considerable danger. As there is marked individual sensitivity to irradiation, there is always the risk of permanent ablation of ovarian function, and therefore its use in such cases is not advised.

*Surgical Treatment.*—Curettage of the uterus is not only diagnostic, and has frequently to be carried out for this purpose, but it is curative in some cases. This being so, it is only reasonable that this simple form of therapy should be employed prior to any more drastic procedure. Hysterectomy is

only indicated after all conservative forms of therapy have failed. It is preferable to the induction of an artificial menopause with radium or deep X-rays in patients under the age of thirty-six, as it is thereby possible to conserve ovarian function, which is an important consideration in women of that age.

**Mid-menstrual or Ovular Bleeding.**—Vaginal bleeding midway between the periods is not uncommon. It is usually very scanty but may be as much as a normal period. It occurs at the time of ovulation and it is believed to be associated with either an endometrial defect or a temporary diminution in the concentration of the oestrogenic hormone in the blood just before this is made good by the developing corpus luteum. It is of no serious significance in the unmarried woman except for its inconvenience, but it may be a cause of sterility in the married woman.

The daily injection of 5 mg. progesterone, or 30 mg. Ethisterone orally, for three days at the mid-menstrual interval, given over a period of three months, may control the bleeding effectively.

**Amenorrhoea.**—Amenorrhoea may represent a physiological condition, may be an expression of a pathological process or a manifestation of a functional disturbance.

Absence of menstruation is physiological before puberty, during pregnancy and lactation, and after the menopause.

Pathological lesions situated in the pituitary, ovaries or uterus may cause amenorrhoea. Systemic diseases, such as anæmia, pulmonary tuberculosis, schizophrenia, decompensated mitral stenosis, toxic goitre and diabetes mellitus, are also recognized as ætiological factors.

Any interference with the function of the anterior pituitary gland and ovaries, which normally control the menstrual process, will upset menstrual periodicity. The autonomic nervous system and the higher cerebral centres dominate in some degree anterior pituitary function. It is not surprising, therefore, that psychogenic disturbances acting through the higher cerebral centre, especially in those susceptible to psychological trauma, adversely affect the hypophyseal secretions. As a general rule the ovaries and uterus in these cases are capable of being stimulated; it is the hormonal stimulus to these structures which is deficient or absent.

**Management.**—A consideration of the ætiological factors involved in amenorrhoea indicates that there is no specific line of treatment, and that only by a review of all the facts accruing from interrogation and examination of the patient can any rational form of therapy be suggested.

In elucidating the patient's history it is important to ascertain if there has been any abnormal psychological stimulus, such as grief, worry, fear, change of surroundings or occupation, etc., within a short time prior to the onset of the amenorrhoea. It is also essential that a careful general examination should be carried out in order that any systemic disease or pathological process, with which amenorrhoea may be associated, may be detected as early as possible. The exclusion of systemic disease or pathological process sometimes demands the radiological and biochemical diagnostic facilities which are only available in a well-equipped hospital. Pregnancy must be excluded in every case. This can readily be done without the patient's knowledge, if there is any doubt, by testing a specimen of urine for the Aschheim-Zondek reaction. Tests for pregnancy are carried out at various Pregnancy Diagnosis Laboratories, in Scotland at the Pregnancy Diagnosis

Laboratory, Usher Institute, Warrender Park Road, Edinburgh. Six oz. of morning urine, without the addition of preservative, should be despatched. The Hogben test gives a result in 24 hours at a cost of 15s., while the Aschheim-Zondek test gives a result in five days at the same cost. The Aschheim-Zondek test is done unless a rapid result is specially requested.

After the exclusion of pathological and physiological causes the amenorrhœa may be considered functional in origin.

Where there is a history of psychological disturbance it is important to explain in simple language to the patient and to her relatives the cause of the amenorrhœa. Furthermore, it is advisable to reassure the patient that the cessation of the menses *per se* does not interfere with general health; nor does it give rise to ill-health in the future. Many amenorrhœic girls are worried regarding their ability, if they marry, to bear children. Marriage, in these cases, should not be discouraged; it often has a beneficial effect on menstrual function. It is always advisable, however, to indicate to the intended husband that whilst the amenorrhœa would not interfere with their sexual life, the likelihood of conception is not so favourable, especially if the girl has never menstruated.

The spontaneous onset of menstruation frequently terminates functional amenorrhœa and this result may be hoped for up to a period of one year. One patient was seen recently who had secondary amenorrhœa of eight years' duration. Menstruation came on spontaneously. After three normal periods there was a further five months' amenorrhœa, and when seen after this interval she was five months pregnant and has since delivered herself of a healthy child. Although menstruation may recur spontaneously after a period of one year, it is not advisable to delay the institution of treatment any longer, and not so long if reassurance does not allay the anxiety.

Before considering any specific therapy it is advisable to concentrate on improving the general health of the patient. As there is a tendency to obesity in many of these cases, a suitable anti-obesity régime should be instituted if required (see p. 383). Conversely, if the patient is markedly under weight, every effort should be made by rest and an adequate diet to promote nutrition. These measures alone, or combined with thyroid medication such as thyroid extract 1 gr. (0.06 gm.) daily, increasing up to 3 gr. (0.2 gm.) daily, are often beneficial.

After a prolonged period of amenorrhœa there is a tendency for the uterus to undergo partial atrophy; it is logical, therefore, to give oestrogenic hormone initially in order to sensitize the uterus and induce uterine development. Five milligrams of synthetic oestrogen are given by mouth thrice daily for a period of ten days. If after a further period of ten days no vaginal bleeding occurs, the same dosage is repeated for another ten days, and so on until bleeding is induced. Except in very resistant patients in whom there may be marked atrophy of the uterus, bleeding occurs six to seven days after the first or second course of therapy. The natural oestrogen, œstradiol benzoate, may be given in place of the synthetic form. It is administered intramuscularly in 5 mg. doses every third day for five injections, and a similar course is repeated after ten days' interval if no bleeding occurs within that time.

The induction of uterine bleeding may be taken as a rough index of full uterine development. Although the bleeding is not normal menstrual loss but is due rather to withdrawal of the oestrogen, it may have a beneficial

psychological effect on the patient, especially where the amenorrhœa is of short duration. It is advisable, however, to follow up uterine bleeding induced by œstrogen by the administration of gonadotrophic hormone since, in the majority of cases, the pituitary stimulus to the ovaries is deficient or in abeyance and must be supplemented. Serum gonadotrophic hormone, 500 I.U., combined with urine gonadotrophic hormone, 200 I.U., is given every third day until five injections have been given. After an interval of ten to fourteen days the same course is repeated. It may be necessary to give several courses of these preparations before any effect is produced, and it is advisable to continue their administration during the first half of the cycle for a period of three months after menstruation has been established. Preparations of serum and urine gonadotrophic hormone are made up in powder form and are supplied with the necessary solvent. It is important that the powder be dissolved completely and that the site of injection be massaged thoroughly, as thereby some unpleasant local reactions may be minimized. It may be that in the past the dosage of gonadotrophic hormones employed has been too low and that better results would be obtained were the dosage markedly increased. High dosages of these preparations, however, are not at present readily procurable.

**Minor Menstrual Disorders.**—Hypomenorrhœa, or scanty menstrual loss, sometimes requires no treatment as it is frequently associated with a normal ovarian and uterine cycle. In such cases conception is possible. Although the loss may be normal or scanty, however, many women have incomplete ovarian and uterine cycles due to a failure of ovulation. This type of menstruation is termed *anovular* and is a causative factor in sterility. It can be detected by the histological examination of the endometrium immediately prior to the onset of menstruation when a pre-ovulatory or proliferative endometrium is found instead of the normal secretory phase, or by the failure to detect pregnanediol in the urine examined during the second half of the menstrual cycle. Further, this type of menstruation should be suspected when there is no rise in the basal temperature recorded daily during the menstrual cycle.

Oligomenorrhœa or delayed menstruation is common and may be associated with a complete or incomplete ovarian or uterine cycle. It is important in that it is frequently associated with lassitude and a feeling of depression and irritability and may be a precursor of amenorrhœa.

Supplementary gonadotrophic therapy is indicated in these disorders as it is probable that they are due to a defective pituitary stimulus to the ovaries. Serum gonadotrophic hormone, 500 I.U., combined with urine gonadotrophic hormone, 200 I.U., should be given intramuscularly every third day for five injections, the first injection being given immediately after the cessation of menstrual loss. This treatment should be continued over three menstrual cycles.

**Dysmenorrhœa.**—The innumerable therapeutic measures advocated for the relief of primary dysmenorrhœa indicate that many ætiological factors have to be considered and that several lines of treatment may have to be adopted before success is obtained. Thus it is evident that there is no single form of therapy suitable for every case. A routine scheme of treatment is recommended, such as the following:—

*General Measures.*—As there is probably a psychological factor operating in the majority of cases, the initial step should include an investigation of this

aspect. It will be found that a brief explanation to the patient of the essentially physiological nature of the menstrual process is often helpful in dispersing the many doubts and superstitions which are founded on a misguided upbringing or unfavourable associations. Every effort should be made to promote a condition of physical fitness, special attention being directed to ensuring sufficient exercise, rest and an adequate diet. As constipation is a very prevalent ætiological factor in the causation of dysmenorrhœa, particularly when present during the pre-menstrual phase, a regular evacuation of the bowels should be ensured by instituting the measures recommended on p. 561. Further, it should be emphasized that, if possible, menstruation should not be allowed to interfere with the normal daily routine and activities. The adoption of these general measures alone often results in alleviation of the menstrual pain.

*Sedative Treatment.*—Mild analgesics, such as aspirin gr. v (0.3 gm.) three times a day, reinforced where necessary by gr.  $\frac{1}{4}$  (15 mg.) codeine or phenacetin gr. v (0.3 gm.), when the pain is severe, are often efficacious. In view of the danger of habit formation it is undesirable to prescribe opiates or acquiesce in the use of any form of alcohol.

*Hormone Therapy.*—If the pain comes on before the onset of the menstrual flow, then it is believed that it is due, in some cases, to an excessive action of the œstrogenic hormone or defective progesterone influence on the uterine musculature. In such cases the administration of 5 mg. progesterone every second day, starting six days before the expected period, or 30 mg. oral progesterone, is often beneficial. Conversely, when the pain coincides with the onset of the menstrual flow, it may be due to an excessive action of progesterone on the uterus, and the administration of 5 mg. of a synthetic œstrogen three times a day for four days before the period is often effective. The treatment in either case should be continued over three menstrual cycles.

*Surgical Treatment.*—When these simple measures fail to relieve the dysmenorrhœa, it is important to carry out a detailed pelvic examination, preferably under anæsthesia, especially in young girls, in order that pathological lesions in the uterus and adnexa may be detected and the appropriate treatment instituted. When no pathological pelvic lesion is present, dilatation of the cervix should be advised, as this is found to be effective in many cases. Severe cases resistant to the lines of treatment already recommended should be referred to a specialist, who may consider the injection of alcohol into the cervical ganglia, paravertebral block or the division of the presacral nerve.

## STERILITY

Sterility may be defined as failure to conceive after a period of three years of normal married life. This interval of time is, however, arbitrary; a barren couple over the age of thirty may require investigation after a much shorter interval.

A detailed history of previous illnesses and a general physical examination is advisable in every woman seeking advice in regard to sterility. It is important to inquire into her menstrual and sexual history. Conditions such as anaphrodisia, excessive coitus, dyspareunia and vaginismus may have an unfavourable effect on conception. A pelvic examination is also necessary



in order to exclude gross lesions of the reproductive tract. The exclusion of systemic disease such as active pulmonary tuberculosis, severe cardiac disease and chronic kidney lesions, is of paramount importance in regard to child-bearing. It requires delicate judgment to decide whether pregnancy is desirable or even advisable in the presence of these constitutional disturbances, and therefore a very thorough initial examination is necessary in order to assess the female partner's fitness for pregnancy and parturition.

If no abnormality can be found in the female, and pregnancy is not contraindicated, then the male partner should be examined before any further detailed investigation is carried out. Examination includes a history of previous illnesses and infections, general examination, examination of the genitalia and of the seminal fluid. The instructions which should be given to the husband regarding the collection of seminal fluid are as follows:—

(1) Three or four days' continence should be observed.

(2) The seminal fluid, obtained either by manipulation or coitus interruptus, should be collected in a small wide-mouthed glass jar which has been very thoroughly washed. The condom or rubber sheath is not suitable for the collection of specimens as the impurities in the rubber and the powder necessary for the use of the sheath interfere with spermatoc motility.

(3) The specimen should be kept at room temperature and examined by a competent pathologist within one or two hours of collection.

The total volume of the ejaculate of a normal fertile male should be 4-5 c.c. with a spermatozoa count of 100,000,000 per c.c. A count below 60,000,000 must be considered unsatisfactory. Twenty per cent. of abnormal forms is within the range of normality. The ejaculate must be free from blood and pus. The spermatozoa retain some motility for a period of four hours after ejaculation.

Azoöspemia or complete absence of spermatozoa in the ejaculate suggests that there is absolute sterility, but several specimens should be examined before this assumption is confirmed. The patient, however, should be referred to a urologist for testicular biopsy in order to determine whether the azoöspemia is due to defective spermatogenesis resulting from atrophy of the seminiferous tubules or to a blockage in the seminal tract. At present there is no effective treatment for the former; occasionally operative treatment is successful for the latter.

Oligospermia or sub-normal spermatogenesis is common, but as many extrinsic factors influence spermatogenesis, a definite diagnosis should be made only after two or more ejaculates have been examined. When a diagnosis of oligospermia is substantiated the most likely beneficial therapy is gonadotrophic hormone given in conjunction with male hormone. Serum gonadotrophic hormone, 500 I.U., combined with chorionic gonadotrophic hormone, 200 I.U., should be given every second day over a period of one month; the course may be repeated after an interval of two or three weeks. Testosterone propionate in large doses depresses spermatogenesis, but small doses of the order of 5 mg. twice weekly may be beneficial. The androgenic hormone does not influence spermatogenesis but stimulates the secretion of the prostate and seminal vesicles and thus creates a more normal seminal pool. This therapy should therefore be given in conjunction with the anterior

pituitary-like preparations. Vitamin E in some form may also prove useful.

When the male has been found to be potent and no gross abnormality can be detected in the female, then the management suggested is as follows:—

The couple should be instructed to make every effort to become as physically fit as possible. They should have sufficient exercise, adequate sleep, and a full diet especially rich in protein. Alcohol and drugs, if not interdicted, must at least be restricted.

They should be advised regarding the optimum time for conception. It is now recognized that ovulation occurs, in the majority of women with a normal 28-day cycle, about fourteen days prior to the menstrual period. It therefore follows that coitus about the 12th-18th day of the cycle, counting the first day of menstruation as day one, gives the best chance for conception. This rule does not obtain for all women and especially those with an abnormal cycle. Information regarding the time of ovulation can be gained, in some cases, by estimating the daily temperature. The rectal temperature, when recorded at a fixed time each morning, is shown to be raised at ovulation and to continue at a slightly higher level until the next period. By charting the daily temperature over several months the approximate time of ovulation can frequently be detected. This applies to an irregular as well as to a regular cycle. A good working rule which applies to all cases is to advise the couple to restrict coitus for the first month to the week immediately after the period; for the second month to the second week after the period, and for the third month to the third week after the period. It is hoped thereby that coitus and ovulation may coincide.

As many barren women have a mild hypothyroidism which is not detectable except by estimation of the basal metabolic rate, it seems rational to give  $\frac{1}{2}$  gr. (30 mg.) thyroid extract daily, increasing the dose by  $\frac{1}{2}$  gr. monthly until  $1\frac{1}{2}$  gr. (0.1 gm.) are taken daily during the third month.

Whilst the physiology of the spermatozoa is not yet fully understood, it is known that the addition of Ringer's Glucose to the seminal pool re-activates many sluggish spermatozoa and may induce the necessary vigour in the spermatozoa for their gyrations through the female genital tract. Accordingly, a pre-coital vaginal douche with 250 c.c. Ringer's Glucose (Sodium Chloride 9.0 gm., Potassium Chloride 0.23 gm., Calcium Chloride 0.22 gm., Glucose (C.P.) 20.0 gm., distilled water to 1,000 c.c.) may have a beneficial effect and should be advised.

Failure to conceive after six months of this régime indicates that further investigation is necessary and the patient should be referred to a specialist. The patency of the fallopian tubes will have to be investigated, and this can be done either by air insufflation or hystero-salpingography after the injection of an opaque substance. Further, the occurrence of ovulation, if not already demonstrated by a record of the basal temperature, will be determined by the estimation of pregnanediol excretion in the urine or by endometrial biopsy. The reaction of the vaginal secretions, seminal fluid and seminal pool require investigation as well as the seminal permeation of the cervical mucus. Dilatation of the cervix alone is frequently a successful therapeutic measure. Artificial insemination may have to be considered in some cases where a structural genital defect in the male precludes normal intromission.

### RECURRENT ABORTION

*General Treatment.*—It is important in the management of a patient who aborts repeatedly that she should have a thorough physical examination prior to the next conception, and any systemic disease treated. Lesions of the reproductive tract such as retroversion of the uterus and cervical lacerations must be corrected. The blood should be tested for the Wassermann reaction, and if positive, specific therapy should be instituted. It is now recognized, however, that syphilis is not a common cause of recurrent abortion. Although so far there is no clear evidence that blood incompatibility is an exciting factor in habitual abortion, it may be advisable to investigate the rhesus grouping of both partners (see p. 937). The patient should be given definite instructions to be followed when conception occurs. She should be advised to lead as quiet a life as possible, avoiding over-exertion and excitement. It is frequently desirable to prescribe a mild sedative such as phenobarbitone  $\frac{1}{2}$  gr. (30 mg.) night and morning. Coitus should be interdicted during the first three months of pregnancy. The importance of rest must be emphasized and complete rest in bed is desirable during the time when the periods would occur had not pregnancy intervened. Attention should be directed to the careful regulation of the bowel in order to avoid the necessity for any drastic purge which may be disastrous. She should be told that any suspicion of vaginal bleeding is an indication for the immediate cessation of all activities.

*Specific Therapy.*—The administration intramuscularly of 10 mg. progesterone twice weekly, or 20 mg. oral progesterone daily, during the first four months of pregnancy, is frequently successful. The same dose should be given thrice daily if bleeding occurs and should be continued until it ceases. There is evidence that in some cases of recurrent abortion the progestational hormone may not be deficient but imperfectly metabolised, which occurrence has the same effect. The imperfect metabolism of progesterone may be due to a relative deficiency of oestrogen, and accordingly it may be advisable to give small amounts of synthetic oestrogen, such as 10-15 mg. daily, concurrently with progesterone. Vitamin E in the form of wheat germ oil concentrate in capsule form or tablets of synthetic *a*-tocopherol is also advocated: the recommended dose of the former is one capsule thrice daily throughout pregnancy and that of the latter one 3 mg. tablet thrice daily for the same period. In cases of suspected hypothyroidism the administration of thyroid extract 5 gr. (0.3 gm.) daily should prove beneficial.

There is some doubtful clinical evidence of the therapeutic effect of urine gonadotrophic hormone in this condition. The dose recommended is 100 I.U. given intramuscularly twice weekly throughout pregnancy.

### THE MENOPAUSE

Some women pass through the climacteric with the minimum of discomfort whilst others have a most distressing and hazardous time. These varying effects are possibly determined, in the majority of cases, by the mental status of the individual.

Although the characteristic menopausal symptoms, such as hot flushes, tachycardia, lassitude, nervousness, irritability, etc., are most frequently

associated with the decline of ovarian function, the possibility of systemic disease such as tuberculosis, hyperthyroidism or anæmia being responsible for these symptoms must not be overlooked. Accordingly, a thorough general examination is necessary prior to the institution of treatment directed towards the relief of symptoms. Irregular uterine bleeding at the menopause should not be considered natural and inevitable until the possibility of malignant disease has been excluded, and this can only be done with confidence by histological examination of the endometrium removed by uterine curettage.

Many women at the menopause are assailed by doubts and fears regarding the future; they believe that they will put on weight, grow hair on the face and become less attractive and that their marital relations and happiness will become strained. These forebodings must be dispelled. It should be explained to them that the change of life is a physiological process and that no ill-effects accrue in the majority of cases, but the importance of leading an active and ordered life at this time should be emphasized. Such reassurance, by itself, or given in conjunction with  $\frac{1}{2}$  gr. (30 mg.) phenobarbitone twice or thrice daily, is usually effective in women complaining of mild subjective symptoms.

Œstrogenic hormone therapy is usually successful in controlling the more severe symptoms directly associated with the menopause. Large amounts of the hormone should be given initially in order to bring the distressing symptoms under control as rapidly as possible, and thereafter the dose should be gradually reduced. The dosage employed should vary according to the severity of the disturbance. In the most severe cases of climacteric disorder the following scheme of treatment is advised. Synthetic œstrogen in 5 mg. doses is given thrice daily by mouth until all the subjective phenomena are completely controlled. Thereafter 5 mg. are given twice daily for one week and once daily for a further two weeks. The dose is then reduced to 1 mg. daily for a further period of two or three weeks. If the synthetic œstrogen is not well tolerated it is necessary to give the natural œstrogen intramuscularly. 5 mg. œstradiol benzoate are given daily until the symptoms are controlled, and this is followed by a gradual reduction in the dosage over the ensuing four to six weeks. The patient should be warned that this treatment may induce uterine bleeding and even some fullness of the breasts. Uterine bleeding induced as a result of this therapy is of no serious significance but calls for cessation of treatment.

Patients who have been left untreated over a period of many years or who develop vasomotor and nervous symptoms years after the menopause, react favourably to the scheme of œstrogenic therapy outlined above, but a maintenance dose of the hormone may have to be given over a very prolonged period.

**Post-Menopausal Disturbances.**—Several conditions may develop at varying intervals after the menopause which may be directly or indirectly associated with cessation of ovarian activity. The most important of these are senile vaginitis, kraurosis vulvæ and pruritus vulvæ. Œstrogenic hormone therapy is specific for senile vaginitis and kraurosis vulvæ, while its administration, if not curative, brings about alleviation in many cases of pruritus vulvæ. A large dose of œstrogenic hormone should be administered, either 5 mg. of a synthetic œstrogen thrice daily by mouth or 5 mg. œstradiol benzoate daily by the intramuscular route. This treatment

usually requires to be continued over a period of ten to fourteen days or even longer according to the severity of the condition and the response to treatment.

### LACTATIONAL DISORDERS

**Stimulation of Lactation.**—Simple measures, such as increasing the fluid intake, hot and cold plotting of the breasts and complete emptying of the breasts after each feed, are usually effective in stimulating an increased flow of milk when the supply is inadequate to meet the needs of the infant. There are some cases, however, in which such measures are ineffective, and it is probable that the mammotrophic or milk-stimulating hormone of the anterior pituitary, prolactin, is deficient. The administration of this hormone is often successful and should always be given a fair trial, when other measures fail, before resorting to artificial feeding. This preparation, Physolactin (Glaxo Laboratories), is in liquid form and is made up in 15 c.c. ampoules. The dosage recommended is 5 c.c. intramuscularly daily for the first two days, 2 c.c. daily for the third and fourth days and 1 c.c. on the fifth day.

**Inhibition of Lactation.**—No woman at the present time need suffer the discomfort of tight binding of the breasts and drastic purging formerly employed to inhibit lactation either early in the puerperium or at the time of weaning of her infant. The inhibition of lactation can readily be accomplished by the administration of oestrogenic hormone, which has an antagonistic action on prolactin, the mammotrophic hormone of the anterior pituitary. An effective dosage is 5 mg. of a synthetic preparation of oestrogen by mouth thrice daily for four days followed by 5 mg. daily for a further six days. Synthetic oestrogens as a general rule are well tolerated during pregnancy and the puerperium and therefore the natural oestrogens need rarely be employed. When breast-feeding is definitely contraindicated oestrogen therapy should be initiated the day after delivery, in which case milk rarely appears in the breasts.

T. N. MACGREGOR.

# DISEASES OF THE BLOOD

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## INTRODUCTION

IT is universally agreed that in all diseases, treatment, to be successful, must be preceded by accurate diagnosis. This is particularly the case in diseases of the blood. In the diagnosis of the anæmias it is not sufficient to rely solely on the symptoms complained of or on the appearance of the patient. The symptoms of all types of anæmia are dependent mainly on anoxæmia, and their severity varies according to the degree of anoxæmia and the rapidity with which it is produced. Similarly, no sign by itself can be held to be diagnostic, and it is unwise to rely solely on the appearance of the skin, especially of exposed surfaces, for diagnosis of the type or degree of the anæmia present. Hence no short-cut to correct diagnosis exists, and a careful blood examination should always be performed when anæmia is suspected. In certain types of anæmia, in which the diagnosis is obscure, examination of the peripheral blood must be supplemented by examination of the bone marrow obtained by sternal puncture. If the general practitioner is unable or unwilling to carry out these investigations he should send a blood smear and a sample of oxalated blood to a laboratory. This should be done prior to the institution of treatment, otherwise essential diagnostic features in the blood picture may be altered to such a degree that the pathologist may have great difficulty in reaching a correct diagnosis. This is particularly likely to occur if the practitioner uses a shot-gun prescription of both iron and liver extract, in which case it may be difficult or impossible to decide which type of therapy should be continued.

That general practitioners still rely largely on a physical examination for the diagnosis of the type of blood disease present, and not on a blood examination, is fully recognized by medical men with special experience in hæmatology. Not infrequently patients report at our blood clinic who have been treated for months or years, at great expense, with liver extract, and who could have been cured with iron in a few weeks at the cost of a few shillings. On the other hand, the majority of cases of pernicious anæmia entering hospital have been diagnosed as hypochromic anæmia and have been treated with iron for months.

Lastly, we wish to stress the need for a thorough investigation into the underlying causal factors. The value of making such investigations is two-fold: first, if the causal condition is not removed, treatment of the anæmia may fail even if the appropriate hæmatonic is given; second, pathological conditions causing the anæmia may advance to an incurable stage if symptomatic treatment for the anæmia alone is prescribed. This is particularly true of malignant disease of the gastro-intestinal tract, where a considerable temporary improvement in the blood picture may result from the administration of iron, despite the progress of the cancer.

So far we have made a plea for full blood examination in every case in which the doctor suspects the presence of anæmia from the symptoms and physical signs, but certain clinical features in the absence of anæmia call

equally for blood investigations. In chronic leukæmias, hæmolytic anæmias, the hæmorrhagic diatheses and agranulocytic angina, anæmia may be absent or mild in degree at certain periods. Accordingly, the presence of enlargement of the spleen, liver or lymph nodes, and unexplained hæmorrhage, sepsis or icterus, indicate the need for a blood examination which should include, in every case, a red and white cell count, hæmoglobin estimation and examination of a stained blood film, and in some cases a differential white cell count, thrombocyte count, reticulocyte count, sternal puncture and other special investigations.

## CLASSIFICATION

Treatment can be placed on a more rational basis if the practitioner has some simple but clear conception of the classification of diseases of the blood. The classification submitted below places the various blood disorders into two main groups: (A) the anæmias, and (B) a miscellaneous group of diseases, some of which are not necessarily accompanied by anæmia, but which are generally dealt with in textbooks of hæmatology.

Group A is divided into three subdivisions. The obvious advantage of this classification is that cases in Group A (I) are treated by appropriate substitution therapy, namely, iron, liver extract, folic acid and vitamin C; cases in Group A (II) by removal of the hæmolytic agent, where possible, or by splenectomy; and cases in Group A (III) by removal of the causal agent, where possible, and by blood transfusion. In Group B the treatment varies in each individual disease.

## THE ANÆMIAS

### I. ANÆMIAS DUE TO DEFICIENCY OF FACTORS ESSENTIAL FOR NORMAL BLOOD FORMATION

#### (a) Iron.

1. Chronic nutritional hypochromic anæmia, including the Plummer-Vinson syndrome, chlorosis, and the hypochromic anæmia of pregnancy.
2. Hypochromic anæmia of infancy and childhood.
3. Post-hæmorrhagic anæmia, acute and chronic.

#### (b) The antipernicious anæmia factor.

1. Addisonian pernicious anæmia.
2. Megaloblastic (pernicious) anæmia of pregnancy.
3. Macrocytic anæmia complicating pathological conditions of the gastro-intestinal tract, *e.g.*, intestinal anastomoses, sprue, idiopathic steatorrhœa, etc.
4. Tropical macrocytic anæmia.
5. Macrocytic anæmia of liver disease.

#### (c) Vitamin C.

Scurvy (dealt with in the section devoted to Deficiency Diseases).

#### (d) Thyroxin.

The anæmia of myxœdema (dealt with in the section devoted to the Endocrine Glands).

## II. ANÆMIAS DUE TO EXCESSIVE BLOOD DESTRUCTION

- (a) Primary hæmolytic anæmia, congenital and acquired.
- (b) Secondary hæmolytic anæmia.
- (c) Paroxysmal hæmoglobinuria.
- (d) The acute hæmolytic anæmia of Lederer.
- (e) Sickle-cell anæmia.
- (f) Hæmolytic anæmias of infancy (dealt with under "Diseases of Infancy").

## III. ANÆMIAS DUE TO APLASIA OR HYPOPLASIA OF THE BONE-MARROW

Aplastic and hypoplastic anæmia.

- 1. Idiopathic.
- 2. Secondary.

## MISCELLANEOUS DISEASES OF THE BLOOD

### I. SPLENIC ANÆMIA (Banti's disease).

### II. POLYCYTHÆMIA.

- (a) Polycythæmia vera.
- (b) Enterogenous cyanosis.

### III. HÆMORRHAGIC DISEASES.

- (a) The purpuras.
  - 1. Primary.
  - 2. Secondary.
- (b) Hæmophilia, hypoprothrombinæmia, fibrinopenia.

### IV. AGRANULOCYTOSIS.

### V. THE LEUKÆMIAS.

### VI. INFECTIOUS MONONUCLEOSIS (dealt with in the section of Infectious Diseases, see p. 34).

### VII. DISEASES OF THE RETICULO-ENDOTHELIAL SYSTEM.

- (a) Reticuloses, including Hodgkin's disease, reticulum cell sarcoma and lymphosarcoma.
- (b) Diseases of lipoid metabolism.
  - (a) Gaucher's disease.
  - (b) Niemann-Pick's disease.
  - (c) Hand-Schüller-Christian disease.

There are certain forms of treatment of particular value for, and commonly employed in, widely differing types of anæmia. In order to save needless repetition regarding technique and dosage, we have dealt with such procedures in great detail in certain sections, and merely refer the reader to the appropriate pages, where they are advised in other forms of anæmia. A full description of iron therapy and the general measures required for the care of a case of anæmia will be found in the section on Chronic Nutritional Hypochromic Anæmia; the indications for, and dangers of, blood transfusion in the section on Acute Post-hæmorrhagic Anæmia; while liver, liver extract and folic acid therapy is described under the heading "Pernicious Anæmia and related Megaloblastic Anæmias."



## THE ANÆMIAS DUE TO IRON DEFICIENCY

### CHRONIC NUTRITIONAL HYPOCHROMIC ANÆMIA

*(Idiopathic Hypochromic Anæmia. Chronic Microcytic Anæmia. Simple Achlorhydric Anæmia)*

Chronic nutritional hypochromic anæmia is the name given by us to the iron-deficiency anæmia occurring chiefly among women of the child-bearing age belonging to the poorest classes of the community. The fundamental factor in its causation is the ingestion of a diet, the iron content of which is insufficient to meet the demands of menstruation and pregnancy. Our investigations in Aberdeen (1935) and Edinburgh (1943) indicate that a subnormal hæmoglobin level is present in some degree in 50 per cent. of working-class women, and 15 per cent. are severely anæmic. The same factors operating in adolescent girls produce an identical anæmia to which the name "chlorosis" is given. In the early part of the century chlorosis occurred with great frequency and severity, but to-day, owing to improved working conditions, it is relatively infrequent and mild in degree. When a woman becomes pregnant, anæmia may develop or become accentuated because of the reduced intake and assimilation of iron from alteration of appetite and diminished gastric secretion of hydrochloric acid, and also because of the foetal demands for iron. In many cases of hypochromic anæmia of pregnancy, however, hydræmia accentuates an anæmia which existed before the pregnancy began. Since exactly the same measures for the prevention and treatment of these three forms of hypochromic anæmia are indicated, it is unnecessary to deal with them individually.

**Prophylaxis.**—The first step is improvement of the diets of women of the poorest classes. While in theory this is easy, it is in practice often extremely difficult, since the principal cause of dietary deficiency lies in the economic field. Hence the family doctor should know the cost and the relative values of the different foodstuffs in regard to their iron content and its availability. Table I gives a list of some of the commoner foods rich in iron and indicates which are the cheapest sources of this mineral. As will be indicated in the section devoted to dietetics, it is far more economical and more efficient to buy medicinal iron from the chemist than to buy food iron from the butcher and the greengrocer. From the point of view of prophylaxis, however, this is not to be recommended, since our dietary surveys have clearly shown that iron is only one of many deficiencies in the diet of the poorest classes. When the iron intake is improved by a selection of foods rich in iron, *e.g.*, liver, meat, pulses and green vegetables, the deficiency of animal protein, calcium, phosphorus, and vitamins is simultaneously corrected. It is only when such a diet is found to be unable to maintain a normal blood level that the administration of medicinal iron is indicated. In women past the menopause we have found that a normal blood level and iron balance can be maintained on an intake as low as 4 mg. of iron daily. Approximately 10 mg. will supply the needs of the majority of women whose menstrual periods are moderate to scanty, or in whom child-bearing is infrequent and not attended by excessive post-partum hæmorrhage. In women with more profuse periods and more frequent pregnancies a dietary intake of 10 mg. daily, or even considerably more, may not maintain a normal blood level. In such cases the administration

of medicinal iron for one week in each month is a cheaper and more efficient method of achieving this result than increasing the iron intake further by dietary means.

The second factor requiring consideration is pregnancy. Since approximately 50 per cent. of women of the poorest classes suffer, during pregnancy and the early puerperium, from some degree of anæmia conditioned by the foetal demands for iron, and post-partum hæmorrhage, it is obvious that the family doctor should be continuously on the outlook for the occurrence of anæmia by examining the conjunctival mucous membrane and by inquiring into such symptoms of anæmia as weakness, dyspnœa and palpitation. Our experience of hæmoglobin estimations at the ante-natal

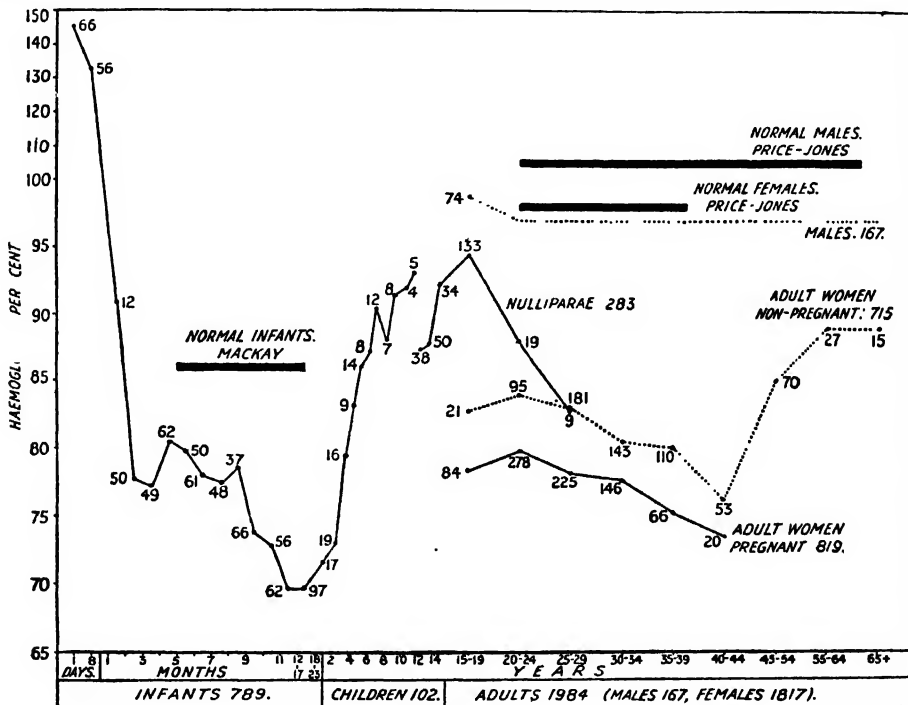


FIG. 3.

Chart showing average hæmoglobin level among poor persons of all ages and both sexes.  
(By courtesy of the "British Medical Journal.")

clinic at Aberdeen strongly suggests the desirability of making this procedure part of the routine examination at all such clinics. In all cases of anæmia, no matter how mild, a month's treatment should be instituted with curative doses of iron, as indicated below, and this should be followed by a maintenance dose (one-third of the curative dose) for the duration of pregnancy and one month afterwards. By such means it should be possible to prevent labour occurring under the dangerous conditions not infrequently seen, where the hæmoglobin level may be 30 per cent. or less. Moreover, should a severe post-partum hæmorrhage occur, the patient might be able to withstand it without being precipitated into a dangerous state of shock.

The third factor to be considered in relation to prophylaxis is menstruation. In women whose diet has been corrected as far as possible in keeping with their economic circumstances, and in whom anæmia develops without

any obvious cause, such as pregnancy, post-partum hæmorrhage, abortion or infection, the most likely cause of the anæmia is menstrual blood loss. In some persons a clear history of menorrhagia is obtained, whereas in others the periods are stated to be normal. Little reliance, however, can be placed on a woman's assessment of her menstrual loss. If it is believed that excessive menstrual blood loss is occurring, it is essential to exclude organic disease of the uterus or adnexæ, and to consider the question of endocrine dysfunction in addition to prescribing prophylactic doses of iron. Before advising curettage for menorrhagia in women already anæmic, a course of iron therapy should be instituted, since correction of the anæmia not infrequently leads to more normal periods. In other cases menstrual loss of blood may not be reduced or may even become more profuse. In such cases either curettage or endocrine treatment may be indicated. If the woman is approaching the menopause, the hastening of this process by irradiation may be advisable.

**Curative Treatment.**—Treatment may be considered under the following heads:—

- (a) General measures.
- (b) Symptomatic treatment.
- (c) Dieto-therapy.
- (d) Iron treatment.

(a) **GENERAL MEASURES** include the provision of physical and mental rest, good nursing, fresh air and sunshine if possible, and the avoidance of chills. If the hæmoglobin level is 40 per cent. or less, the patient should be confined to bed. Since the blood level falls very slowly and the blood volume is maintained in chronic nutritional hypochromic anæmia, the patients become to a considerable extent acclimatized to a low level of hæmoglobin. (This is in contrast to the state of shock which occurs in patients with a sudden external loss of blood, even though the hæmoglobin has fallen only to 50 or 60 per cent.) Hence it is unnecessary for the patient to be at complete rest in bed; she may assume the position she finds most comfortable and sit up in bed for her meals. Usually such patients defæcate more regularly if they are allowed to go to the lavatory, and this may be permitted if it is in close proximity to the bedroom and on the same floor. Alternatively a bedside commode may be used. When the hæmoglobin has reached 50 per cent., the time allowed out of bed should be increased and graduated exercise should be ordered, particular care being taken to avoid undue fatigue or chilling owing to the liability of anæmic individuals to develop infections. Until iron treatment has corrected the anæmia, rest in bed is the best form of treatment for alleviating the symptoms of anoxæmia, circulatory instability, and myocardial weakness, namely, dyspnœa, palpitation, giddiness, etc.

(b) **SYMPTOMATIC TREATMENT: GASTRO-INTESTINAL SYSTEM.**—Gastro-intestinal disturbances are frequently present. Anorexia, often of many years' duration, occurs in many patients. A feeling of weight and discomfort in the epigastrium after meals, nausea, vomiting, flatulence, constipation and periodic attacks of diarrhœa are other symptoms. A rapid improvement in all such symptoms may be expected within a week or two of the start of iron therapy, especially if the patient is confined to bed on a light diet. Nevertheless it is often desirable to give symptomatic treatment while awaiting the effects of iron therapy. In some patients with dyspepsia

and flatulence associated with achlorhydria and chronic gastritis, beneficial results occur from the administration of an alkaline powder : —

R<sub>7</sub> Sod. Bicarb.  
 Bism. Carb.  
 Mag. Carb. Pond. . . . . āā oz. 2 (62 gm.)

Sig. 1 teaspoonful in water three times a day after food.

In other cases a teaspoonful of the powder in a tumblerful of warm water should be taken on awakening in the morning and before going to sleep at night, with the object of loosening the excess of mucus in the stomach. Dilute hydrochloric acid has been used extensively in the treatment of dyspepsia and diarrhoea associated with achlorhydria. It is very doubtful if this treatment has any beneficial effects, and this is hardly surprising since it has been shown that the amount of hydrochloric acid necessary to bring about a significant change in the pH of the gastric contents is many times greater than the pharmacological dose. Accordingly we have not used hydrochloric acid for this purpose for many years. The majority of patients are constipated owing to the poor tone of the musculature of the alimentary tract and lack of vitamin B and roughage in the diet. When the patient is very anæmic and is suffering from anorexia, it is not advisable to treat the constipation by adding large amounts of fruits and vegetables to the diet, because this may cause dyspepsia; nor is it advisable to give purgatives, because they increase small-intestinal hurry and so reduce the absorption of iron. Mineral oils with the addition of agar, with or without a small amount of cascara sagrada or senna, should be prescribed. Emuls. paraff. liq. c. agar (B.P.C.) and emuls. paraff. liq. c. phenolphthalein et agar are suitable for this purpose. Occasionally it may be necessary for the first few days to wash out the colon with saline in the morning, a few ounces of olive oil having been introduced into the rectum the night before. For the atonic constipation so frequently present in these anæmic women we have found yeast to be of considerable value. Vitamin B not only helps constipation by improving the tone of the bowel, but promotes appetite and improves absorption. Two or three yeast tablets three times a day before meals are in our experience an excellent tonic. Many doctors think that iron has a constipating effect, and this may be the case with the small doses of iron formerly used. In the dosage used to-day iron usually has a laxative effect and may even cause pain and diarrhoea if maximal doses are taken from the start.

*The Tongue.*—In the majority of cases the lingual changes are those of an atrophic glossitis with little or no pain. For this condition no symptomatic treatment is required and regeneration of the epithelium may be expected to occur as a result of iron treatment.

In some cases the tongue is red, inflamed and painful (acute generalized glossitis). In other cases painful fissures or ulcers, and fissuring of the angles of the mouth (angular stomatitis) are present. These changes are probably due to a long-continued deficient intake of members of the vitamin B<sub>2</sub> complex, especially nicotinic acid, riboflavin and folic acid. A well-balanced diet supplemented by iron will usually cause a disappearance of these features within a period of a week or two. Should this not occur, a daily supplement of yeast or liver by mouth, foods which are rich sources of the vitamin B<sub>2</sub> complex, should be given. In the very severe case of acute glossitis it may be advisable to prescribe nicotinic acid (two 50-mg.

tablets thrice daily), riboflavin (5 mg. daily) or folic acid (5 mg. daily) individually or in combination for a week. During the acute stage of glossitis the diet must be bland and fluid, and the use of a glass tube to enable the patient to take the food directly to the back of the pharynx may be helpful. Fortunately the condition settles down rapidly when the blood begins to improve.

*Dysphagia.*—A mild degree of dysphagia frequently occurs. This requires no special treatment as it improves *pari passu* with the hæmoglobin level. Should the dysphagia be more severe and persistent, the passage of a mercury bougie may be necessary. In a small proportion of cases difficulty in swallowing is due to a mechanical cause, namely, a web occluding the inlet to the œsophagus. In at least half a dozen of our patients an œsophagoscope had to be passed and the membrane ruptured or cut.

*Nervous System.*—Numbness and tingling in the extremities are common complaints. In the majority of cases no special treatment is required, since the condition disappears as a result of iron therapy. In more severe cases the parenteral and oral administration of vitamin B preparations is of value. Suitable preparations of vitamin B for oral and parenteral use can be obtained from any first-class chemist. For oral treatment yeast in tablet form, marmite or bemax are satisfactory preparations, and for parenteral treatment the subcutaneous injection of 5 mg. of thiamin daily for one or two weeks is usually sufficient.

In view of the anoxæmia of the central nervous system and the anxiety state resulting from the struggle for existence to which many women of the poorest classes are submitted, it is not surprising that many patients are nervous, worried, easily upset, suffer from headaches and sleep badly. Small doses of chloral hydrate, gr. xv (gm. 1) at night, or phenobarbitone,  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) night and morning, are of great value in obtaining the mental and physical relaxation which is so desirable.

(c) *DIET-THERAPY.*—In severely anæmic patients with anorexia, nausea and possibly vomiting, no attempt should be made at this stage to give a diet rich in iron or roughage. A bland, easily digested diet is recommended, divided into small meals at two to two-and-a-half hourly intervals. The basis of the diet should be milk and milky foods, jellies and custards, lightly boiled or scrambled eggs, pounded fish, purées of fruit and vegetables and small amounts of thin bread and butter. Patients in the severely anæmic stage with marked gastric disturbances require hospitalization for nursing and dietetic reasons. With the rise of the hæmoglobin level appetite and digestion improve, and the diet should be cautiously increased by the addition of chicken and meat, vegetables and raw fruit. Our aim is to reach a diet containing at least 10 mg. of iron a day. The optimal intake of iron is stated to be 15 mg. daily, but the economic circumstances of the poor classes may not always permit the purchase of such a diet. Should it be found that the normal requirements for iron conditioned by pregnancy or menstruation cannot be satisfied by a maintenance diet containing approximately 10-15 mg. of iron a day, the administration of medicinal iron for one week in each month must be advised after the normal hæmoglobin level has been restored.

No attempt should be made to bring the hæmoglobin level to normal by dietetic measures alone, since we have shown that this is both uneconomic and unsatisfactory. This does not mean that we should be content with low iron diets (5 to 8 mg. daily), since a figure of at least 10 mg. daily can

be attained cheaply and easily by a proper selection of foods. In addition, an improvement in the protein, mineral and vitamin content will result. Accordingly Table I is submitted in order to indicate the articles of diet most suitable for this purpose. A study of Table I shows that the flesh foods, eggs, oatmeal, lentils, split peas and national bread (80 to 85 per cent. extraction) are articles of food particularly rich in iron. It does not follow, however, that the efficacy of any foodstuff in promoting hæmoglobin regeneration depends solely on its iron content. The availability of the contained iron, which in turn depends on the ease with which ionizable iron is liberated by the processes of digestion, is a factor of great importance. Fortunately it has been found that in general the foods richest in iron have also the highest content of available iron, and accordingly all that the family doctor need know is the list of the foods of a high total iron content included in Table I.

TABLE I  
*Iron Content of the Cheaper Foodstuffs*

Foodstuff.	Total Iron (mg. per ounce).	Cost per lb.*	Mg. of Iron for 1d.
<b>1. <i>Flesh Foods—</i></b>			
Liver, ox, raw . . . . .	3.9	1s. to 1s. 2d.	4.8
Sausage, beef, fried . . . . .	1.1	4d. to 8d.	2.9
Beef, raw . . . . .	1.1	6d. to 10d.	2.2
Corned beef, tinned . . . . .	3.1	7½d. to 10d.	5.8
Rabbit, stewed . . . . .	0.5	2½d. to 5d.	2.1
Herring, fried . . . . .	0.5	1d. each	1.8
White fish, steamed . . . . .	0.2	8d. to 10d.	0.3
Egg . . . . .	0.8	1d. to 1½d. each	1.3
Cheese . . . . .	0.2	6d. to 8d.	0.5
<b>2. <i>Cereals, etc.—</i></b>			
Oatmeal . . . . .	1.2	1½d. to 2d.	11.0
National bread, 85% extraction (1942-1944) . . . . .	0.5	2¾d.	2.9
National bread, 80% extraction (1945) . . . . .	0.3	2¾d.	1.7
White bread, 70% extraction . . . . .	0.2	2½d.	1.3
Rice, polished . . . . .	0.1	2d. to 3d.	0.6
Golden syrup . . . . .	0.4	3d. to 4d.	1.8
<b>3. <i>Vegetable Foods—</i></b>			
Lentils, raw . . . . .	2.2	2d. to 2½d.	15.6
Split peas, raw . . . . .	1.3	2½d. to 3½d.	6.9
Cabbage, raw . . . . .	0.3	1d. to 1½d.	3.8
Leeks, raw . . . . .	0.4	1½d. to 2d.	3.7
Potato, raw . . . . .	0.2	½d. to ¾d.	5.1
Carrot, raw . . . . .	0.2	2d. to 3d.	1.3
Onion, raw . . . . .	0.1	2d.	0.8
Turnip, raw . . . . .	0.1	½d. to ¾d.	4.2
Apple, raw . . . . .	0.1	1d. each	0.3
Orange juice, raw . . . . .	0.1	1d. each	0.2

\* The prices given above are pre-1940.

As the economic factor is of such importance we have shown in column 4, Table I, the amount of iron in milligrams which can be purchased for one penny, and we draw particular attention to the cheapness of "food iron" in oatmeal, lentils and split peas. The costs of the different foods, on which the figures in column 3 are based, were obtained directly from the shops used by the poorest classes in Aberdeen in 1937.

(d) **IRON TREATMENT.**—It is now generally agreed (a) that iron is absorbed in the ferrous state mainly from the duodenum and upper jejunum; (b) that the ferrous salts are more efficacious than the ferric salts; (c) that organic preparations of iron (*e.g.*, hæmoglobin and bone-marrow, etc.) are valueless; (d) that much larger doses are required to obtain optimal results than was formerly believed; and (e) that parenteral iron therapy is attended by considerable danger and discomfort, and at present should seldom be advised. While many preparations of iron are now known to be satisfactory, a comparison of their efficacy, their dosage and cost, is a matter of great interest and importance.

Provided that inhibitory factors such as sepsis, toxæmia or hæmorrhage are absent, a rise of at least 1 per cent. per day in the hæmoglobin level should result from efficient iron therapy. Our investigations have definitely shown that the following preparations in the dosage mentioned may all be considered satisfactory, since a rise in hæmoglobin value of more than 1 per cent. daily resulted from their administration: iron and ammonium citrate, gr. 30 (1.8 gm.) three times a day in a fluid mixture; ferrous sulphate, gr. 3 (0.18 gm.) three times a day after food in tablets. In certain resistant cases the dose should be doubled.

Since both the above preparations are of equal potency in the doses mentioned, it would seem not unreasonable to base one's selection on their convenience, palatability and cost. With regard to convenience, the tablets of ferrous sulphate are superior to the fluid preparations, because they are more portable and do not blacken the teeth and tongue. In addition, a small bottle containing 100 ferrous sulphate tablets will last a month, whereas equivalent treatment with iron and ammonium citrate in the form of a mixture would require renewal of the prescription several times, resulting in inconvenience and repeated payment of the dispensing fee. From the point of view of palatability both are satisfactory, and the choice depends on individual preference. If dysphagia is present, fluid mixtures are obviously preferable. Cure of the anæmia may be achieved with either of these products at a cost of a few shillings.

When the preparation of iron to be administered has been selected, it is inadvisable to start treatment with the full curative dose, since in some individuals this may result in dyspepsia, vomiting or diarrhoea. Accordingly a test dose of one-third of the curative dose should be given for a day or two, and if no gastric symptoms result this should be increased to the full dosage. If some dyspepsia occurs the final dose should be reached by gradual increases over a few days. If dyspepsia persists and is considered not to be functional in origin, it may be necessary to try another preparation of iron. Ferrous sulphate "Emplets" (Parke, Davis & Co.), each containing 5 grains (0.3 gm.), may succeed where other preparations have failed, since they are enteric-coated and so do not dissolve in the stomach. In this connection it is important to realize that the dyspepsia may be a symptom

of the anæmia itself, in which case persistence of iron medication is the correct way of accomplishing its relief.

Lastly, iron should always be prescribed to be taken after meals and followed by a drink of water, as by this means the irritating effects of the mineral on the gastric mucosa are reduced to a minimum.

*Parenteral Iron Therapy.*—The oral administration of iron produces such satisfactory results that parenteral therapy is very rarely indicated. This is fortunate since parenteral administration may cause reactions which may be unpleasant or highly dangerous. Parenteral treatment may be required for the anæmic patient who has a true idiosyncrasy to iron when given orally. Patients are frequently referred to us by their family doctors with the statement that they cannot take any preparation of iron by mouth. In the vast majority of cases explanation, persuasion and insistence on attention to the points discussed in the preceding paragraphs, successfully overcome the so-called idiosyncrasy. Parenteral iron therapy, however, may be required in the rare case of hypochromic anæmia which fails to respond to adequate oral therapy with iron and vitamin C because of malabsorption or for reasons not understood.

The maximal dose of injectio ferri (B.P.), namely 30 minims, contains the equivalent of gr.  $\frac{1}{10}$  (6 mg.) of iron, a quantity totally insufficient to cause a satisfactory rate of hæmoglobin production. Recently it has been shown that saccharated oxide of iron in a 5 per cent. sucrose solution can be given intravenously to man in quantities containing up to 500 mg. of iron. Reactions occur on occasions when the amounts injected are above 100 mg. of iron. Since iron given parente ally appears to be effectively utilized, there seems no object in giving more than 100 mg. of iron at one injection. Two cases of idiopathic iron-refractory hypochromic anæmia under the care of the senior author responded excellently to the intravenous injection of saccharated oxide of iron although all types of iron preparations given by mouth over a period of years had failed to raise the hæmoglobin level above 50 per cent. The recently introduced proprietary preparation Ferrivenin (Benger's Ltd.) has been found by us to be effective and not to cause reactions in doses up to 200 mg. daily. Further investigations into the indications and dangers of intravenous iron medication are required before it should be employed by general practitioners.

*Duration of Iron Therapy.*—The period which will elapse before a normal blood count is attained will vary from one to three months in individual cases, depending on the initial blood level. Treatment should be continued in full therapeutic doses for one month thereafter, in order to provide adequate stores of iron. In women past the menopause maintenance treatment is in general not required, because of their decreased demands for iron. In individuals still menstruating a tendency to relapse is frequently present. If the periods are profuse or pregnancy occurs, iron treatment on the lines laid down in the section devoted to Prophylaxis should be instituted. In those with normal or scanty periods it is unnecessary to continue iron treatment, provided that re-examination for the appearance of anæmia is undertaken at six-monthly intervals. By these means the administration of iron with its attendant cost and trouble to many women who would not relapse is avoided. The recommendations regarding diet, and the factors causing anæmia outlined in the section on Prophylaxis, are equally applicable to the prevention of relapse.



**Vitamin C.**—Vitamin C is recognized as one of the essential factors necessary for normal hæmopoiesis. It has been shown that the anæmia of scurvy will respond to the administration of vitamin C but not to iron. In some cases of iron deficiency anæmia without frank manifestations of scurvy, but where the dietary history suggests the possibility of sub-clinical scurvy, a supplement of ascorbic acid may augment the hæmatinic effects of iron or may initiate a response which has not been produced by iron alone. It must be pointed out, however, that it is unnecessary to prescribe ascorbic acid in the great majority of cases of iron deficiency anæmia if a satisfactory diet is taken. Accordingly it is a wise practice to make sure that all cases of iron deficiency anæmia take a diet rich in vitamin C or alternatively receive a daily supplement of ascorbic acid.

Recent work suggests that ascorbic acid may augment the absorption of iron by virtue of its action as a reducing agent. In the rare case of iron deficiency anæmia refractory to iron alone, the effect of prescribing ascorbic acid in a dose of 50 mg. t.i.d., *given at the same time as the doses of iron*, should be tried.

#### NUTRITIONAL HYPOCHROMIC ANÆMIA OF INFANCY AND CHILDHOOD

Since an adequate store of iron in the foetal liver is of some importance in maintaining a satisfactory blood level in infancy, careful attention should be directed to the provision of a well-balanced diet for the pregnant mother, and the administration of iron should be undertaken if anæmia is present during pregnancy. Such measures are desirable not only from the point of view of prevention of anæmia in the infant but probably also as a means of improving its general nutrition.

A rapid fall in the hæmoglobin level occurs during the first two months of extra-uterine life. No method of treatment can prevent this fall, which appears to be physiological. Recovery normally occurs during the next eighteen months, but there are two factors of particular importance which may prevent or retard this improvement. The first of these is low birth weight occurring as a consequence of prematurity or otherwise. All children of low birth weight should receive iron therapy from the second month. The second indication for prophylactic iron therapy in infancy is the presence of infections. Even mild infections may cause anæmia and retard blood regeneration—hence the administration of iron for some weeks following infection is a sound general rule. Since mild degrees of anæmia have been shown to be frequent in infants of the poorer classes between six and eighteen months, even in the absence of low birth weight and obvious infections, it is probable that at this age-period nutritional factors are also of importance, namely, undue delay in the change from a milk to a mixed diet and the poor quality of the mixed diet which is given. Accordingly the practitioner would be well advised to institute iron therapy in all cases where the infant appears to be pale, easily fatigued and not thriving.

**Iron.**—A palatable, efficient and non-irritating preparation of iron in liquid form which can be added to the infant's feeds is the ideal. For a child of three to six months,  $1\frac{1}{2}$  gr. (0.09 gm.) of iron and ammonium citrate in water sweetened with glycerin, three times a day, is a satisfactory preparation for prophylactic use. The dose should be 3 gr. (0.2 gm.) three times a day if anæmia has already developed. For children of six to eighteen months the prophylactic dose is 3 gr. (0.2 gm.), while the curative dose

varies from 5 to 10 gr. (0·3 to 0·6 gm.) thrice daily. The ferrous salts of iron have been shown to have a higher percentage utilization than the scale preparations, and in our opinion are preferable, since they are equally efficacious in smaller doses. It must be remembered that their efficiency is rapidly reduced if oxidation to the ferric state occurs. Accordingly they must not be prescribed in simple watery solutions but should be mixed with 50 per cent. glucose, which retards oxidation. According to Helen Mackay, the addition of a trace of hypophosphorus acid enhances this effect. She has found the following prescription to be both palatable and effective in the treatment of established anæmia. 1½ gr. (0·09 gm.) of ferrous sulphate is therapeutically equal to approximately 15 gr. (0·9 gm.) of iron and ammonium citrate.

R7 Ferrous sulphate . . . . .	1½ gr. (0·09 gm.)
Dilute hypophosphorus acid . . . . .	¼ m. (0·014 c.c.)
Dextrose . . . . .	15 gr. (0·9 gm.)
Chloroform water . . . . .	to 1 fl. dr. (3·6 c.c.)

Sig., 1 fl. dr. (3·6 c.c.) three times daily.

Whatever preparation of iron is used, treatment should be started by giving doses of one-third to one-half of what is ultimately desired, and the material should be mixed with the feed or given at the end of a feed.

Copper, manganese and some other minerals are believed by certain workers, on the basis of laboratory research in animals, to be necessary for normal hæmopoiesis. Of these minerals the claims of copper alone may be said to have received complete acceptance. It promotes the full utilization of iron in the formation of hæmoglobin by a catalytic action. Because only traces are required it is extremely doubtful if there is any need for its addition to preparations of iron, since our investigations have shown that even in the diets of the poorest classes adequate quantities are present for this purpose. There is some evidence, however, that certain cases of nutritional anæmia in infancy respond better to iron and copper than to iron alone, though this is not the experience of Helen Mackay or ourselves. Should the practitioner desire to give copper as well as iron, certain proprietary preparations are available, such as the ferrous sulphate tablets marketed under the name of fersolate by Glaxo Laboratories, which contain traces of copper and manganese. The difficulty of giving iron in tablet form to infants may be overcome by crushing the tablet immediately before use and mixing it with a feed. Recent reports from America claim that preparations of iron fortified with molybdenum may be effective in hypochromic anæmia resistant to iron therapy. Molybdenized iron is not on sale in Great Britain at the time of writing. ■

### POST-HÆMORRHAGIC ANÆMIA

Extra-vascular blood loss may be acute or chronic. It is necessary to describe the treatment of these two conditions separately, because the mechanism of their symptomatology and the treatment are entirely different.

#### ACUTE POST-HÆMORRHAGIC ANÆMIA

Acute post-hæmorrhagic anæmia is due to the sudden loss of a large amount of blood or to repeated smaller hæmorrhages occurring in rapid succession.

**Treatment.**—This will be described under the following headings: (a) Arrest of Hæmorrhage and (b) Treatment of Shock.

*Arrest of Hæmorrhage.*—In some cases hæmostasis may be secured by ligature of or pressure on the bleeding point—for example, a severed artery, extra-uterine gestation or the bursting of a superficial varicose vein. In other cases, such as in hæmorrhage from a peptic ulcer, it may be possible to ligature the ruptured vessel, but usually this procedure is not indicated. Lastly, the hæmorrhage may be part of a general blood disease such as thrombocytopenic purpura, hæmophilia or acute leukæmia, where mechanical arrest of the hæmorrhage may be impossible.

*Treatment of Shock.*—The degree of shock which follows a sudden loss of blood depends on several factors. The principal ones are: the amount and rate of blood loss, the age and previous health of the patient and, in accidents and major operations, the concomitant effects of tissue trauma and previous exposure to cold. Since the decision to give intravenous fluids depends on a proper appreciation of these factors, it is desirable that they should be elaborated.

The sudden loss of 500 c.c. of blood will not produce symptoms of shock in a healthy adult, as is clearly indicated from everyday experience with blood donors. When symptoms arise they are usually psychological in origin rather than the result of lowered blood volume. Definite symptoms of shock appear when 1,000 c.c. of blood is lost rapidly, and a fatal result may occur if the figure approaches 2,000 c.c. If the loss is spread over twenty-four hours the symptoms are less severe and the prognosis correspondingly better. Infants and old people stand acute hæmorrhage relatively badly, and this is particularly true if there is a history of previous debility or ill-health.

A patient suffering from acute post-hæmorrhagic anæmia and shock should immediately be placed in bed between blankets. A suitable dose of morphia should be injected subcutaneously and repeated in two hours if necessary. The amount required is the minimal quantity necessary to allay apprehension and restlessness, and to control pain if present. Excessive doses of morphia are harmful because of its depressant effect on the respiratory centre. A quarter of a grain (16.2 mg.) for an adult and  $\frac{1}{12}$  to  $\frac{1}{8}$  gr. (5.4 to 10.8 mg.) for a child is sufficient for the initial dose. The foot of the bed should be raised on blocks, the patient being kept flat on his back except for a low pillow under his head. In severely exsanguinated patients awaiting blood transfusion, the limbs should be bandaged with crêpe bandages from below upwards. The body heat should be restored by placing hot bottles along both sides of the body, due care being taken not to burn the patient, whose threshold for pain may be raised owing to collapse, by ensuring that the bottles are well covered by flannel and are not too hot. When available, a radiant heat cradle should be used, as a more even warming of the body can be obtained without the danger of burning the patient. The temperature should be controlled so as to avoid excessive sweating, which would increase the fluid loss and thus further deplete the blood volume. Cardio-respiratory stimulants are frequently ordered in cases with severe collapse while awaiting the assembly of the apparatus necessary for intravenous transfusion. Liq. extract pituitary (B.P.) 1 c.c. subcutaneously, strychnine  $\frac{1}{32}$  to  $\frac{1}{16}$  gr. (2 to 4 mg.) subcutaneously and nikethamide 2 c.c. intramuscularly are used for this purpose, and

the dose may be repeated in two to four hours. These preparations may also be used alternately. Consideration of the mechanics of the circulation in post-hæmorrhagic shock suggests that these drugs are unlikely to be of value and may actually be harmful. As a compensation for blood loss, generalized vasoconstriction occurs spontaneously in an attempt to maintain the blood pressure at a level which will ensure adequate blood supply to the vital centres. Accordingly there appears to be little object in giving the vasoconstrictor drugs adrenaline and pituitary extract. Likewise, the stimulants nikethamide and strychnine are unlikely to be efficacious since the heart and vital centres of the brain are already doing their utmost to maintain a satisfactory circulation and respiratory exchange.

Since the essential cause of shock in acute hæmorrhage is the resulting low blood volume, the restoration of the blood volume is undoubtedly the most important therapeutic procedure required. When shock is only mild in degree, all that may be necessary is an adequate amount of water by mouth. One pint of fluid per hour, for three or four hours, may make good the deficiency. If the degree of shock is more severe, fluid must be given intravenously (*vide* Technique). For this purpose saline, glucose saline, gum saline, plasma or serum (fresh or reconstituted from the dry state) and blood are available. Of the fluids mentioned, blood must take first preference, since it is of the correct viscosity and osmotic pressure and the contained corpuscles effectively increase the oxygen-carrying capacity. Second in order of merit is plasma or serum. If none of these is available, gum saline (6 per cent. gum acacia in normal saline) should be used, because the gum holds the fluid within the vessels for a considerable time. On the other hand, saline and glucose saline pass into the tissue spaces within a few minutes of their injection and hence cannot be recommended for the restoration of blood volume, although they are of the greatest value in correcting the dehydration with loss of chlorides which occurs in excessive vomiting and diarrhoea. A pint of blood will raise the hæmoglobin level and blood volume by approximately 10 per cent. with a concomitant rise of blood pressure. One, two, or more pints of blood should be introduced, the amount depending on the severity of the shock and the degree of anæmia present. Similar quantities of gum saline are indicated if blood is not available.

Blood transfusion should preferably be given by the continuous-drip method, as by this means 2,000 to 3,000 c.c. of blood can be introduced over twenty-four hours with complete restoration of the blood volume and with the lowest possible risk of producing acute heart failure and pulmonary oedema, or causing aggravation or recurrence of the hæmorrhage due to a sudden increase in the blood pressure. If only a tube and funnel are available, it is advisable to limit the amount of blood to 1 to 2 pints, to introduce the fluid very slowly (forty-five minutes per pint) and to repeat the operation if necessary in from four to six hours. In a healthy person suffering from hæmorrhagic shock as the result of an accident or a wound the first pint may be given in fifteen minutes.

When the bleeding point has been effectively secured and the state of shock adequately treated, recovery will occur without further intravenous therapy. On the other hand, when the bleeding point cannot be secured it is usually desirable to make immediate arrangements for finding a suitable

donor even if the initial degree of shock is not marked, since recurrence or increase in the severity of the hæmorrhage may suddenly precipitate the patient into a dangerous state of collapse.

It is now necessary to discuss the indications for blood transfusion. First, it is unwise to rely solely or mainly on a blood count, since for some hours after acute hæmorrhage the hæmoglobin and red cells per c.mm. of blood may be little altered. Moreover a falling hæmoglobin does not necessarily connote continued hæmorrhage. Accordingly an estimation of the degree of shock with its concomitant fall in blood volume should be based on the following clinical signs: sighing respiration, coldness and clamminess of the skin, pallor, general weakness, impairment of mental faculties, rapidity and reduced volume of the pulse and fall in the blood pressure. When the pulse-rate is over 100 and the systolic blood pressure below 90 mm. Hg., a considerable degree of shock is present. It has been calculated that the blood volume is less than 60 per cent. of normal when the systolic blood pressure falls below 80 mm. Hg., and the prognosis is very grave unless immediate blood transfusion is given.

It should be remembered that the great strain on the cardiovascular system, which occurs in severe post-hæmorrhagic anæmia, necessitates the continuation of complete rest in the recumbent position, warmth and good nursing for at least a week after restoration of the blood volume. Thereafter treatment comprises removal of the causal condition where possible and the application of the measures already given in detail in the section devoted to chronic nutritional hypochromic anæmia under the headings General Measures, Dieto-therapy, and Iron.

#### CHRONIC POST-HÆMORRHAGIC ANÆMIA

**Treatment.**—The treatment of chronic blood loss is considered under two headings: (a) Removal of the Causal Condition, and (b) Treatment of the Anæmia.

*Removal of the Causal Condition.*—The most frequent cause of this form of anæmia, especially in males, and the one most likely to be missed, is occult bleeding from the gastro-intestinal tract. We have not infrequently seen patients with hæmoglobin levels below 30 per cent. who were unaware that they were losing blood by this route. The occult bleeding may come from varicose veins in the œsophagus and stomach, peptic ulcers of stomach or duodenum, malignant tumours or polypi of the gastro-intestinal tract, hæmorrhoids or infestation with animal parasites, particularly ankylostomata. Attention is drawn to the great value of the benzidine reaction for the recognition of occult blood in the stools. More obvious causes of chronic blood loss are repeated nose-bleedings, excessive hæmorrhage from the uterus resulting from the presence of tumours, polypi or endocrine dysfunction, and chronic blood diseases such as purpura, hæmophilia and scurvy. In the great majority of cases of obscure hypochromic anæmia the gastro-intestinal and urogenital tracts should first be investigated as possible sources of hæmorrhage. When the cause of the hæmorrhage has been discovered, treatment directed to its removal must be instituted. It should be noted that the diet frequently prescribed for diseases of the gastro-intestinal tract is often low in iron and may accentuate the anæmia if not adequately reinforced with medicinal iron.

*Treatment of the Anæmia.*—This consists of the administration of full doses of iron together with the general measures outlined under chronic nutritional hypochromic anæmia (see pp. 466-472). If the source of bleeding has been removed, the chances of relapse after the blood count has been brought to normal are insignificant and therefore, in general, maintenance treatment with iron is not required.

## PERNICIOUS ANÆMIA AND RELATED MEGALOBlastic ANÆMIAS

It is necessary to emphasize that there are many types of macrocytic anæmia which differ widely one from another in their ætiology, blood picture and response to treatment, excluding the common factor of increased diameter of the erythrocyte. Although the terms "megalocytic" and "macrocytic" are often regarded as interchangeable, it would be convenient if "megalocytic" were restricted to those anæmias associated with a megaloblastic bone-marrow and therefore caused by deficiency of the specific anti-anæmic factor. We believe it is preferable to replace the term megalocytic anæmia by megaloblastic anæmia. The term "macrocytic" could then be used to cover all anæmias characterized by an increased mean cell diameter, including the "megaloblastic" group. If this is accepted, it is possible to divide all macrocytic anæmias into two groups.

Group I comprises the megaloblastic anæmias which develop from a deficiency of a factor necessary for normal blood formation. This factor is probably folic acid, a member of the vitamin B complex.

Group II consists of those anæmias in which the macrocytosis results from causes other than a deficiency of folic acid; it is a more ill-defined and heterogeneous group of relatively rare macrocytic anæmias resulting from widely differing causes. The macrocytosis is secondary, in the majority of cases, to prolonged stimulation or irritation of the bone-marrow. Blood formation proceeds on a normoblastic basis, but owing to its excessive activity the parent cells in the bone-marrow are primitive normoblasts and as a result many of their offspring entering the peripheral circulation are larger and more immature than normal erythrocytes. Macrocytic anæmias belonging to Group II are present in (a) some cases of hæmolytic anæmia—for example, acholuric jaundice, sometimes of the congenital but more usually of the so-called "acquired" type; (b) occasionally in malignant malaria and lead poisoning; (c) not infrequently in acute leukæmia and in the terminal stages of chronic leukæmia; and (d) in cases of Hodgkin's disease and malignant disease, in which the bone-marrow is irritated by metastatic deposits. These macrocytic anæmias are differentiated from the true megalocytic anæmias on four main grounds: (a) the finding of the ætiological factor; (b) by full examination of the blood picture, which differs in important details in regard to red cells, white cells and platelets; (c) by sternal puncture, which will show a normoblastic, not a megaloblastic, hyperplasia; and (d) by their failure to respond to the ingestion or injection of liver or folic acid and by their response to appropriate treatment (splenectomy, X-rays, etc.).

It is hoped that the preceding remarks make it clear that all megalocytic anæmias are macrocytic, but that all macrocytic anæmias are not

megalocytic. The following discussion will be restricted to the treatment of pernicious anæmia and other megaloblastic anæmias.

#### CLASSIFICATION OF THE MEGALOBLASTIC ANÆMIAS

The specific anti-anæmic factor, a deficiency of which leads to megaloblastic blood formation, is probably folic acid, a member of the vitamin B<sub>2</sub> complex. This substance occurs in food in a conjugated form which cannot be utilized by the bone-marrow until it is transformed into free folic acid. This transformation depends on the availability of a factor which is produced in the stomach as the result of the action of a gastric enzyme (intrinsic factor) on certain foods (extrinsic factor) and is absorbed from the intestine and stored in the liver. It is obvious that a deficiency of folic acid may arise in one of five ways: (a) by a failure in the production of the factor required for the liberation of free folic acid from its conjugate; (b) by a defective intake of conjugated folic acid in the food; (c) by a failure in absorption of folic acid; (d) by ineffective storage in the liver of folic acid or the factor which liberates it in the free form; (e) for reasons as yet not understood (see idiopathic refractory megaloblastic anæmia, p. 485).

Under (a) are included Addisonian pernicious anæmia and some cases of the megaloblastic pernicious anæmia of pregnancy. In the former the loss of the specific gastric enzyme (intrinsic factor) is permanent, while in the latter it is temporary. Some cases of the megaloblastic anæmia of pregnancy are refractory to the injection of potent liver extracts and in these it is assumed that factors (b) and (c) also operate. We also include under (a) the megaloblastic anæmias which result occasionally from extensive resection of the stomach or its widespread destruction by cancer.

Under (b) is included the nutritional megaloblastic anæmia commonly seen in tropical and semi-tropical countries, particularly in pregnant women (Wills) and also in non-pregnant women and men, which arises from direct dietary deficiency and not from a failure in gastric secretion.

Under (c) is included the megaloblastic anæmia which occurs in many cases of tropical and non-tropical sprue, and in some cases of pellagra. In certain instances dietary deficiency and impairment of gastric secretion are factors to be considered in addition to a failure in absorption. Occasionally absorption is so seriously affected in individuals suffering from intestinal stenosis, from multiple anastomoses and from prolonged diarrhoea, as to result in a megaloblastic anæmia.

Under (d) are included cases of severe liver disease, particularly cirrhosis, in a proportion of which, estimated by various authors at from 5 to 25 per cent., a macrocytic anæmia occurs. In some of these cases cell volume measurements show that this is really a false macrocytosis due to flattening of the cells produced mechanically during the spreading of the blood film. It is suggested that the physical state of the plasma in cirrhosis conduces to this effect. In other cases, however, cell volume measurements are in agreement with cell diameter measurements indicating the presence of true macrocytosis. It should be noted that a typical megaloblastic marrow is very rarely encountered in the macrocytic anæmia associated with liver disease. When this is found it is presumed that the damage to the liver prevents it functioning efficiently as a storage organ for folic acid or the liberating factor discussed above. In such cases the administration of folic

acid or liver extract by mouth or by injection may cure or improve the anæmia, but will not alter the underlying disease of the liver.

The value of such a classification lies in the fact that all cases of macrocytic anæmia with a megaloblastic marrow falling under (a), (b), (c), (d) and (e) are examples of anæmias due to a specific deficiency of folic acid and as such can confidently be expected to be relieved by supplying the missing factor. Since Addisonian pernicious anæmia is the most common and the most important of the megalocytic anæmias, it will be used as the example on which treatment of all the megaloblastic anæmias can be modelled, with suitable modifications.

### PERNICIOUS ANÆMIA

The aim of treatment is (1) to restore the blood picture, qualitatively and quantitatively, to normal as quickly as possible; (2) to maintain a normal blood level; and (3) to replenish and stock adequately the depots of the body with the factors necessary for blood formation. Minot has rightly pointed out that the individual who receives only just enough of a nutritional factor, such as a vitamin or a mineral, to maintain health, may be precipitated into the zone of partial deficiency with the advent of infection: hence the importance of adequate reserves.

It would appear advisable to consider the treatment of pernicious anæmia according to the stage of the disease present when the patient is first seen. The value of folic acid in pernicious anæmia and allied megaloblastic anæmias is discussed on p. 486.

**The Severe Relapse Stage.**—The patient is critically ill and in a collapsed state, with a blood count of approximately 1 million red cells and a hæmoglobin content of 20 to 30 per cent. Before 1926, patients were frequently seen in this terminal stage, but to-day there can be no possible excuse for allowing such a state to develop. The question of blood transfusion immediately arises, and the clinical condition of the patient, as judged by the degree of circulatory failure rather than by the blood level, must be the deciding factor (see p. 476). If it is concluded that the delay of four or five days which must elapse before improvement can occur as a result of treatment entails a risk to life which should not be taken, a blood transfusion should be given at once.

The decision is often a difficult one to make. Undoubtedly blood transfusion in such severely anæmic patients should not be undertaken without a full realization of the risks involved, the most important of which is the possible occurrence of acute pulmonary œdema and death. This catastrophe is due to a failure of the weakened myocardium to withstand the effects of the increase in blood volume which accompanies transfusion. Accordingly we believe that transfusion of concentrated red-cell suspension (that is, citrated blood from which most of the plasma has been removed) is better than the use of whole blood. In this way the number of red cells in the circulation may be increased with relatively little increase in the blood volume. The packed red cells should be transfused very slowly, one pint (*i.e.* the red cells derived from approximately two pints of blood) being given in not less than six hours, or one half-pint given in not less than two hours on each of two successive days. In less urgent cases, in which some doubts exist regarding the need for immediate transfusion, a suitable donor



should be procured and arrangements made to have him available immediately an emergency arises.

An extract suitable for intramuscular injection should be injected into the gluteal region (*e.g.*, 4 c.c. campolon, or 2 c.c. anahæmin, hepastabforte, neo-hepatex, or Lederle's liver extract). The intramuscular injection of liver extract in the doses mentioned above should be continued daily for three or four days, by which time the reticulocyte increase and a marked subjective improvement will be noted. Within ten days the blood count should have risen by nearly 1 million red cells and the patient should be out of all danger.

*Iron.*—A preparation of iron (see p. 470) should be given twice a day after meals and continued for two months, in all cases receiving treatment by the parenteral route, since an iron shortage is apt to arise owing to the exceedingly rapid production of erythrocytes. Iron may increase the anorexia and dyspepsia so frequently present in the severe relapse stage of pernicious anæmia, and accordingly the administration should be delayed till after the occurrence of the reticulocyte crisis, by which time the marked clinical improvement of the patient will enable it to be well tolerated.

*Hydrochloric Acid.*—Hydrochloric acid, combined with glycerin of pepsin is commonly prescribed if dyspepsia or diarrhœa is present. For the reasons stated on p. 467 it is of doubtful value.

It should be pointed out that the most efficacious treatment for all the symptoms of pernicious anæmia and for the prevention of such serious complications as spinal cord degeneration and disease of the gall-bladder is the parenteral administration of adequate amounts of liver extract. Dyspepsia, diarrhœa, sore tongue and general weakness all disappear in the majority of cases without any symptomatic treatment.

*General Measures.*—Diet, rest, nursing, etc.—see pp. 466-469 for full details. If there is reason to suspect a deficiency of vitamin C, ascorbic acid (50 mg. t.i.d.) should be given for a fortnight, as there is evidence to show that such a deficiency may retard or even inhibit the response to parenteral liver therapy.

*Stage of Moderate Relapse.*—The patient complains of weakness, palpitation, exhaustion, dyspepsia and dyspnœa on effort, but there is no immediate danger to life. The blood count may be from  $1\frac{1}{2}$  to  $2\frac{1}{2}$  million red cells and the hæmoglobin 40 to 60 per cent. In such a case a choice must be made between parenteral and oral treatment.

*Parenteral Treatment.*—An intramuscular injection of liver extract in the doses already mentioned should be given on three or four consecutive days, deeply into the gluteal region, alternating daily from side to side. Following the injection, firm massage should be applied to the site for a few minutes (for a full description of the technique of intramuscular injections, see p. 944). By this means subsequent pain and stiffness are greatly reduced. Thereafter, a weekly injection must be given until the blood count is normal. It not infrequently happens that the blood level tends to become stationary around  $3\frac{1}{2}$  to 4 million red cells and 80 to 85 per cent. hæmoglobin and the patient looks and feels perfectly well. This is sometimes due to the presence of factors inhibiting blood regeneration such as arteriosclerosis or chronic sepsis and hæmorrhage. It is essential to restore the blood level completely to normal (5 million red cells and 100 per cent. hæmoglobin), as this is important in preventing degenerative changes in the spinal cord, and it may

be necessary at this stage to double or treble the number of weekly injections before normality is attained.

No special diet is required. The patient should take a plentiful, well-balanced, mixed dietary, containing red meat, liver or kidney and green vegetables in at least one meal a day.

*Drugs.*—Iron as already indicated.

*Oral Treatment.*—Liver extract by mouth was the treatment of choice prior to 1932. The extract from 500 gm. of liver daily is generally needed to obtain maximal regeneration of the blood. As the cost of treatment works out at from 20s. to 30s. weekly, compared with approximately 5s. when parenteral treatment is given, liver extract by mouth can no longer be recommended, for economic reasons. In addition, in resistant cases and in those in whom absorption is poor, oral treatment does not compare with parenteral, on the grounds of efficiency. Half a pound daily of lightly cooked liver is the average dose required, if liver is taken in the crude state. Since the anti-anæmic factor is moderately heat stable, there is no point in prescribing raw liver. There are several reasons why the ingestion of liver cannot be recommended as the treatment of choice: first, there is an ever-increasing difficulty in obtaining regular and adequate supplies; secondly, the cost of liver has risen very greatly; and thirdly, many persons fail to continue to take the amount required to attain and maintain a normal blood level, owing to the nausea and disgust engendered by the constant sight, taste and smell of the article.

*Hog's Stomach Preparations.*—These preparations are insoluble and contain the gastric enzyme, which is thermolabile; hence they must not be heated. Excellent results can be obtained from the use of desiccated stomach (B.P.C.) and such preparations as ventriculin, pepsac, ektomak, etc., in doses of a tablespoonful three times a day, in water, milk, orange juice, etc. English preparations such as pepsac are relatively cheap, but they have an unpleasant taste and smell, which can be improved, however, by exposing the next day's ration to the air for twelve hours in a saucer covered with muslin.

*Pre-operative Measures.*—Should an emergency arise during the relapse stage of pernicious anæmia, requiring an operation which cannot be delayed, intensive parenteral treatment should be undertaken immediately (5 c.c. of liver extract intramuscularly, repeated in twelve hours), and a suitable donor should be procured in order that a blood transfusion can be immediately given if required. Patients in the remission stage of pernicious anæmia, particularly if they show signs of neurological disease, should receive double or treble the usual quantity of liver extract for a few days before undergoing any major operation, since the blood level tends to fall and neurological degeneration to progress after serious surgical procedures.

Chronic focal sepsis (in tonsils, teeth, or accessory sinuses) should not be treated radically until there has been an adequate response to specific anti-anæmic therapy. On the other hand, localized and easily accessible collections of pus should be evacuated, since they tend to inhibit or retard the therapeutic response.

*Maintenance Treatment.*—Since liver treatment does not produce a cure, but is a form of substitution therapy, maintenance treatment must be continued for life. This point should be carefully explained to patients, who will then be unlikely to neglect reporting regularly for the necessary treat-

ment; and it should be noted also by all doctors because, as we have found, some are liable to increase the intervals between injections excessively, reduce the quantity of liver injected or cease injections altogether after a remission has been induced by the initial course of treatment.

The amount of material required to maintain a normal blood level varies greatly in different individuals, often for no apparent reason. Only by trial, checked by blood counts, can the problem of dosage be satisfactorily settled, and this applies equally to the stages of remission and relapse. For maintenance treatment the necessary number of intramuscular injections of liver extract varies in different individuals from one a week to one every six weeks. In our experience an average dose is 5 c.c. of campolon or 4 c.c. of anahæmin, or the other more concentrated extracts already mentioned, at intervals of approximately four weeks. Iron is not required if it has already been prescribed during the first two months of treatment. An ordinary well-balanced mixed diet is all that is required. The maintenance dose of liver and hog's stomach preparations is also extremely variable in different individuals; on the average it may be said to be 2 lb. of liver or 4 oz. of dried hog's stomach preparation weekly.

The depot storage method of treatment, whereby 5 to 10 c.c. of a liver extract is injected intramuscularly on two consecutive days, is of value to patients proceeding on holiday or on business to places where facilities for treatment are not available. By this method a satisfactory blood level may be maintained over periods up to three months.

**Sensitivity to Liver Extract.**—A small proportion of patients undergoing parenteral liver therapy develop allergic reactions which may be mild (flushing, tachycardia and localized urticaria) or so severe as to endanger life (generalized urticaria, severe bronchospasm, collapse). The reactions occur within 5 to 30 minutes after injection. Treatment consists of the immediate injection of adrenaline, repeated as required. Although occasionally subsequent injections of liver extract may not be followed by reactions, in general it is wise to decide whether to continue parenteral therapy after desensitization or to replace it by the oral ingestion of liver, liver extract, proteolyzed liver, folic acid or hog's stomach preparations. So great are the advantages of parenteral liver therapy that we believe that desensitization should be undertaken where suitable facilities and personnel are available for this potentially dangerous procedure. Desensitization can be accomplished by giving increasing doses of liver extract parenterally at intervals of days or weeks or by completing the process within a few hours as described below. We have arbitrarily divided sensitive patients into two classes: (1) those with mild symptoms; (2) those with severe constitutional reactions.

**Mild Cases.**—It is permissible in mild cases to attempt to control the reactions by injecting 3 minims (0.17 c.c.) of 1 in 1,000 adrenaline hydrochloride concurrently with the liver preparation. In some cases this may be sufficient without any alterations or addition to treatment. In other cases satisfactory results may be obtained by reducing the quantity injected to one-half or one-quarter of the dose which produced a reaction and decreasing compensatorily the periods between injections. Adrenaline may be given at the same time. After a few weeks on this treatment the dose per injection and the intervals between injections can be gradually increased to the desired maintenance levels.

**Severe Cases.**—The degree of sensitivity is assessed by the history of

the severity of the generalized reaction and by the response of the skin and the patient to an intradermal test of 0.05 c.c. of the liver extract to be used. If any generalized reaction occurs to this test, desensitization should be started with a smaller quantity of liver extract, such as 0.01 c.c. In the great majority of cases 0.05 c.c. will be found to be a suitable initial dose. With the initial and all subsequent injections, 0.3 c.c. of adrenaline hydrochloride (1 in 1,000) is given. The same dose of adrenaline should also be given between each injection of liver extract if reactions occur at any stage of desensitization. The dose of liver extract is doubled every half-hour and the route of the injection is changed from the intradermal to the subcutaneous when the 0.4 c.c. dose of extract has been reached, and to the intramuscular route at the 1 c.c. dose. It is our experience that if a reaction is going to occur during desensitization it generally follows the 1 c.c. dose. In this event the same dose is repeated in half an hour, and if no reaction occurs the dose is increased to 1.5 c.c. and finally to 2 c.c. of extract at half-hourly intervals. In the majority of cases desensitization is secured in three to five hours. Thereafter it is advisable to repeat the final dose (2 c.c.) daily for three days without the addition of adrenaline. Weekly doses of 2 c.c. are now given for six weeks, and finally maintenance therapy is continued by a single injection once every two, three or four weeks. We advocate the daily and weekly injections mentioned above because we have found that there is a tendency for sensitivity to recur if the interval between the initial course of desensitization and the next injection is delayed for two weeks or longer. Although Kaufman *et al.* (1943) advise that the intervals between injections for maintenance treatment should not exceed one week, since otherwise sensitivity will recur, this has not been our experience, as we have at the present time many patients who have been desensitized and who have maintained a normal blood level for several years without a recurrence of sensitivity on an intramuscular injection of anahæmin monthly.

*Antihistamine Drugs* (Anthisan, Benadryl, etc.).—Recent work carried out in Edinburgh has shown that the dangers mentioned above may be greatly reduced or obviated by the administration of antihistamine drugs prior to and during the process of desensitization. (For details of technique and dosage see p. 99.)

### SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

**Prophylaxis.**—Lesions of the cord rarely if ever develop in pernicious anæmia if the blood level is maintained within normal limits. It must be emphasized, however, that the symptoms of a patient having maintenance treatment for pernicious anæmia cannot be relied upon as an indication of the blood level. Many patients receiving inadequate maintenance therapy complain of no symptoms although the blood count may be definitely subnormal, *e.g.*, Hb. 80 per cent., R.B.C. 3.5 to 4 million. It is in such cases that the incidence of subacute combined degeneration of the cord is highest. It is of great importance, therefore, that blood counts should be done at regular intervals (preferably every three months) during maintenance treatment, unless the expensive policy of giving excessive amounts of liver extract is followed. If the red cell count falls below 4.5 million in the case of women or 5 million in men, or if examination of a blood film shows the

presence of macrocytes although the blood count is above those levels, maintenance treatment is inadequate and should, therefore, be increased. Our experience has convinced us that the danger of degeneration of the spinal cord is obviated by observance of these precautions. The danger of spinal cord lesions developing when folic acid is employed as the sole therapeutic agent for initial and maintenance treatment is referred to on p. 487.

**Treatment.**—The treatment of established subacute combined degeneration is discussed in the section devoted to diseases of the nervous system (see p. 891). All that need be said here is that cases of pernicious anæmia with signs of neurological involvement should receive from two to three times as much of the anti-anæmic factor as cases with a comparable blood picture but without neurological changes. In addition, it is wise to supplement parenteral treatment with oral liver therapy, hog's stomach preparations and vitamin B (yeast, marmite, etc.). This intensive treatment should be continued for at least six to twelve months after the blood count has reached normal and should be combined with remedial exercises. By these means many cases which are bedridden may be able to lead a useful life, while patients with less severe involvement of the spinal cord may return to full employment. The failure of folic acid to prevent subacute combined degeneration is discussed on p. 487.

### MEGALOBlastic ANÆMIAS OTHER THAN ADDISONIAN ANÆMIA

The scheme of treatment outlined above is satisfactory for the treatment of the anæmia present in the other conditions mentioned, with the following modifications.

#### MEGALOBlastic (PERNICIOUS) ANÆMIA OF PREGNANCY

We prefer the term "megaloblastic anæmia of pregnancy" for this group to the commoner name "pernicious anæmia of pregnancy" because some cases have a colour index of unity or slightly below and the feature common to all the cases is a megaloblastic bone-marrow.

Many cases respond satisfactorily to injections of liver extract in doses similar to those required in Addisonian pernicious anæmia. We have found, however, that some patients fail to respond to parenteral therapy or do so only after a variable period during which blood transfusions may be necessary to maintain life. Satisfactory remissions can usually be induced in these cases by the ingestion of  $\frac{1}{4}$  to  $\frac{1}{2}$  lb. (0.11 to 0.22 kg.) whole liver daily or  $\frac{3}{4}$  to  $1\frac{1}{2}$  oz. (23.3 to 46.6 gm.) of proteolyzed liver or oral liver extract daily (see p. 485) or 10 mg. daily of folic acid. In the majority of cases treatment can be discontinued after the puerperium and the restoration of a normal blood level.

#### TROPICAL AND NON-TROPICAL SPRUE

The introduction of folic acid has greatly simplified the treatment of tropical sprue. Within a week of starting treatment with 10 mg. folic acid daily by mouth the stool becomes formed, abdominal distension is reduced and a marked improvement in appetite and sense of well-being occur. The dietetic restriction of fat formerly recommended need not

be so strict. Plenty of first-class protein is still advisable. If the anæmia is of the megaloblastic type, a rapid improvement in the blood picture occurs. Many chronic cases of the sprue syndrome, however, have a moderate degree of macrocytic anæmia with a normoblastic marrow. In such cases folic acid may fail to restore the blood picture qualitatively or quantitatively to normal. Oral liver extract or proteolyzed liver (1 oz. daily by mouth) should then be tried and in some cases will be successful. The results of treatment with folic acid or liver extract in idiopathic steatorrhœa are usually much less satisfactory than in tropical sprue although on occasions equally dramatic effects are produced. Maintenance treatment with folic acid is required in many cases, otherwise a clinical relapse will occur. The dosage needed for this purpose is variable, but is probably around 5 mg. daily. In celiac disease the anæmia is usually hypochromic and the bone-marrow frankly normoblastic. In our experience folic acid has been ineffective in improving the anæmia or controlling the steatorrhœa. In the occasional case in which the bone-marrow is megaloblastic, excellent results have been reported. For further information about the sprue syndrome see p. 488.

#### MACROCYTIC ANÆMIA OF HEPATIC DISEASE

In the macrocytic anæmias occurring in cases of severe liver disease, the results of anti-anæmic treatment are often unsatisfactory, since prognosis depends on the degree and progress of liver damage. If treatment with iron and parenteral liver extracts fail, proteolyzed liver (see p. 485) and folic acid (see p. 486) should be given a trial.

#### IDIOPATHIC REFRACTORY MEGALOBlastic ANÆMIA

The term "refractory anæmia" was coined by Bomford and Rhoads to describe certain severe types of anæmia which failed to respond to all recognized forms of hæmatinic treatment. On the basis of sternal puncture findings the refractory anæmias have been classified by Davis and Davidson into two main groups. In one, the bone-marrow is hypocellular, all elements being reduced. Erythropoiesis is normoblastic, and the blood picture may be either normocytic or macrocytic. In the second group, which was less frequently encountered, the marrow was hypercellular and megaloblastic, the blood picture being essentially megalocytic, resembling that of pernicious anæmia.

The first group comprises classical aplastic and hypoplastic anæmia (see p. 494). Cases belonging to the second group may develop secondarily to pregnancy, sprue, idiopathic steatorrhœa or other derangement of the gastro-intestinal tract, as indicated above, or may occur idiopathically. Such idiopathic cases, despite a megaloblastic marrow, are refractory to parenteral liver therapy, and death from anæmia may occur unless life is maintained by repeated blood transfusion. The recent introduction of proteolyzed liver and folic acid (see p. 486), however, has altered the prognosis of refractory megaloblastic anæmia, since a dramatic response may be anticipated within a week of starting treatment. Satisfactory results have also been obtained from the administration of liver or liver extract given orally. Proteolyzed liver is a fat-free papain digest of fresh liver,

consisting of a powder easily soluble in water which is given in doses up to half an ounce thrice daily. It contains some hæmatinic principle which is destroyed or removed during the chemical preparation of parenteral liver extracts. It is sold under the trade-name Hepamino (Evans Ltd.). Analysis has shown that in addition to the amino-acids derived from the breakdown of liver protein, proteolyzed liver is a rich source of the various members of the vitamin B complex including folic acid, and this may partly explain its therapeutic action in the megaloblastic anæmias.

### THE RÔLE OF FOLIC ACID IN THE TREATMENT OF ANÆMIA

The name "folic acid" was originally given to a substance isolated from spinach. It has been shown to be present in the green leaves of other plants and also in mushrooms, yeast and in animal tissue such as liver and kidney. Folic acid is a member of the vitamin B<sub>2</sub> complex and is an essential factor required for the growth of certain bacteria such as the *lactobacillus casei* and for the normal growth and development of a variety of animals. Of particular interest is the experimental finding that a deficiency of folic acid leads to a depression of production of erythrocytes, leukocytes and thrombocytes in certain animals. The clinical implications of this work were immediately recognized by physicians, but therapeutic trials were unsatisfactory until the synthesis of folic acid by Angier in 1945 resulted in the production of adequate amounts of the vitamin of constant composition for clinical trial. In 1946 synthetic folic acid was marketed by the Lederle Company of America under the trade name Folvite. It is supplied in ampoules for parenteral injection and in tablets for oral ingestion. Each tablet contains 5 mg. of folic acid. At the time of writing, Folvite is available to practitioners in Great Britain at a high price, but it can be confidently expected that in due course the price will be reduced as supplies increase. As already indicated on p. 478, it is now generally believed that the specific anti-anæmic factor which is necessary for the continuation of normoblastic blood formation, and a deficiency of which leads to megaloblastic blood formation, is free folic acid. On this basis all types of megaloblastic anæmia, however produced, should respond to folic acid therapy, and this has in fact been shown to be the case. The amount of folic acid required for initial treatment and maintenance treatment has not been finally established. The senior author has had excellent hæmopoietic responses in pernicious anæmia from the oral administration of folic acid in doses varying from 20 mg. to 1 mg. daily. The suggested initial dose for the treatment of all types of megaloblastic anæmias is 10 mg. daily for ten days and 5 mg. daily thereafter until the blood count is normal. For maintenance treatment the requirements have not been finally established. Probably they lie in the region of 2½ to 5 mg. daily. However, for reasons given below, folic acid alone cannot be recommended for the maintenance treatment of pernicious anæmia. There is no object in using the parenteral route as oral administration is simpler and probably more effective, even in the sprue syndrome. We have given folic acid in a single dose of 400 mg. by mouth and 200 mg. by intramuscular injection. No unpleasant reactions were produced and an excellent hæmopoietic response resulted. Large single doses are, however, wasteful and extravagant since their effect in raising the blood level continues only for about two or three

weeks, and a much larger gain in red cells and hæmoglobin can be obtained if the same amount of material is given in divided doses of 5 to 10 mg. daily.

**Addisonian Pernicious Anæmia.**—The hæmatological effects produced in Addisonian pernicious anæmia appear to be identical with those resulting from parenteral or oral liver therapy. The question therefore arises as to whether folic acid should be recommended as the therapeutic agent of choice in pernicious anæmia. The advantage to the patient of replacing parenteral therapy by the ingestion of a small tablet daily is obvious. The disadvantages are the present high price of the material and the risk of the patient failing to take the daily dose regularly through carelessness or ignorance. It has been established that while folic acid will restore the blood count to normal and maintain it there, it will neither prevent nor cure subacute combined degeneration of the cord. Hence it is imperative to stress that for the maintenance treatment of pernicious anæmia reliance must still be placed on liver therapy, and particularly on parenteral liver therapy. Further information must be obtained before it can be decided whether a combination of folic acid and parenteral liver extract is more effective than either preparation given alone. It is possible but not certain that the amount of liver extract required to maintain the integrity of the central nervous system is less than the amount required to maintain a normal blood level. If this was shown to be the case the quantity of liver extract required might be reduced or the intervals between injections prolonged, if folic acid was being taken simultaneously. In the writers' opinion the advantages of parenteral liver therapy so outweigh those of folic acid that it appears doubtful if the latter preparation will ever play a significant rôle in the treatment of Addisonian pernicious anæmia. The increase in the blood level resulting from a single injection of 2 c.c. of a potent purified liver extract in the relapse stage of pernicious anæmia is as great as that obtained from the daily intake of 5 to 10 mg. of folic acid for 14 days. Most cases of pernicious anæmia on maintenance treatment remain in perfect health and with a normal blood count when given 4 c.c. of liver extract approximately every four weeks. There appears to be little justification for supplementing liver extracts with folic acid since patients with pernicious anæmia must be able to ingest and absorb sufficient conjugated folic acid from an ordinary mixed diet; otherwise parenteral liver therapy would be ineffective, since purified liver extracts probably act by liberating free folic acid from its conjugate (see p. 478). Only when anorexia, vomiting or diarrhœa have been prominent features for a considerable time prior to treatment being commenced in the relapse stage of pernicious anæmia would there appear to be an adequate reason for combined treatment with folic acid and liver extract, and then only for a few days until the patient was able to partake of a good mixed diet. Folic acid can be recommended as a temporary measure for cases of pernicious anæmia who have become sensitized to parenteral liver extracts, since we have found that no such reactions occur when folic acid is given either parenterally or orally. Desensitization, as described on page 482, must ultimately be carried out if parenteral liver therapy is to be continued. If this is deemed undesirable the combination of folic acid and oral liver therapy can be recommended. Folic acid therapy can be used as a temporary measure for patients who are going on holiday or for business purposes to places where it may be difficult to receive their routine injections of liver



extract. The conclusion we have reached at the time of writing is that the injection of parenteral liver extract still remains the best method of treatment for pernicious anæmia at all stages of the disease, and that folic acid should be used only as a temporary measure and for the particular purposes discussed above.

**Other Megaloblastic Anæmias** (*Nutritional Megaloblastic Anæmia, Idiopathic Refractory Megaloblastic Anæmia, Pernicious Anæmia of Pregnancy, and the Sprue Syndrome*).—Since the megaloblastic transformation of the bone-marrow in this group of anæmias is conditioned mainly by a defective intake or absorption of conjugated folic acid in the food, it is not surprising that the injection of purified liver extract which contains no folic acid is often partially or totally ineffective. In all such megaloblastic anæmias folic acid will initiate a hæmopoietic response. Similar results can usually be obtained by the ingestion of liver in amounts up to  $\frac{1}{2}$  lb. (0.22 kg.) daily, or oral liver extract or proteolyzed liver in doses of 1 oz. (31.1 gm.) daily. Critically ill patients with anorexia and gastro-intestinal dysfunction find it much easier and pleasanter to swallow a small tablet of folic acid than to take the requisite amount of the above liver preparations. Since subacute combined degeneration of the cord seldom, if ever, develops in any type of megaloblastic anæmia other than Addisonian pernicious anæmia, initial treatment can be safely undertaken with folic acid. In nutritional megaloblastic anæmia and the megaloblastic anæmia of pregnancy, folic acid therapy can be stopped when the blood level has returned to normal provided a satisfactory diet is eaten. In idiopathic refractory megaloblastic anæmia and in some cases of the sprue syndrome, maintenance treatment must be continued for life. The maintenance dosage of folic acid has not yet been established, but we have reason to believe that it may lie between  $2\frac{1}{2}$  and 5 mg. daily. It is probably wise to supplement folic acid with oral or parenteral liver therapy for maintenance purposes since we have had several cases of the sprue syndrome which developed severe peripheral neuritis while taking folic acid alone.

**Normoblastic Anæmia, Leucopenia and Thrombocytopenia.**—The presence of a normoblastic bone-marrow reaction indicates that no deficiency of folic acid is present. It is not surprising, therefore, that the administration of folic acid has been found to be totally ineffective in all forms of anæmia with normoblastic blood formation. Such anæmias include iron deficiency anæmias, the hæmolytic anæmias and the leucopenias. The senior author has treated a large series of cases of aplastic anæmia, thrombocytopenia and leucopenia, some of which were idiopathic in origin and others secondary to recognized toxic or infective causes. In no instance was any benefit secured, a result which is particularly regrettable since no specific drug is available for the cure of these serious conditions.

## HÆMOLYTIC ANÆMIAS

The hæmolytic anæmias include a group of anæmias of widely differing causation, the essential diagnostic feature of which is the presence of excessive blood destruction as demonstrated by the finding of bilirubinæmia, urobilinuria and an excess of immature circulating erythrocytes (reticulocytes) in the presence of a stationary or falling blood count. This term should not be applied to the mild hæmolytic phenomena which occur in

the severe relapse stage of the megalocytic anæmias, such as pernicious anæmia, sprue, etc. In such diseases the anæmia is not mainly due to hæmolysis, but to disturbed erythropoiesis, whereas in the true hæmolytic anæmias hæmolysis is the essential factor in the production of the anæmia.

True hæmolytic anæmias can be divided into two groups:—

**Primary.**—Where the fault lies in the formation of defective erythrocytes which are peculiarly susceptible to destruction by the cells of the reticulo-endothelial system, especially in the spleen.

**Secondary.**—Where the hæmolysis results from direct injury to normal cells by extraneous toxic or infective factors, and where it occurs, often from unknown causes, as an accompaniment of certain diseases such as carcinomatosis.

The need for this subdivision is apparent if intelligent treatment is to be prescribed, because in the first group the abnormal erythropoiesis cannot be altered by any known method, and treatment consists essentially of reducing blood destruction by splenectomy; while in the second group the aim is the removal or neutralization of the toxic or infective factors together with symptomatic treatment of the anæmia.

### PRIMARY HÆMOLYTIC ANÆMIAS

Under this heading are included familial acholuric jaundice (hæmolytic icterus, congenital hæmolytic anæmia) and acquired (idiopathic) hæmolytic anæmia. In no other blood disease is there a greater need for accurate diagnosis than in the primary hæmolytic anæmias, since the course is not influenced materially by drug or dietetic treatment but only by splenectomy. The reader is referred to textbooks of hæmatology for details of the investigations necessary to establish the diagnosis.

**Familial Acholuric Jaundice.**—The problem of treatment resolves itself into a simple one, namely, whether splenectomy should be undertaken and, if so, when. Considerable divergence of opinion exists in this matter, particularly in mild forms of the disease, where the patient is “more jaundiced than ill.” Many authorities believe that splenectomy should be advised in every case when the diagnosis is made, because of the occurrence of serious complications in a high percentage of cases, at some later period in the disease. The principal complications which may endanger life and greatly enhance the risk of operation are cholelithiasis and cholecystitis, severe hæmolytic crises and a terminal exhaustion of the bone-marrow. On the other hand, since the familial form of the disease has been recorded in successive generations in individuals who were able to carry on their occupations with little or no ill-health, other authorities do not consider that splenectomy is indicated in the milder cases of this group. Our own feeling is that, since it is impossible to foretell with certainty the future of even the mildest case of acholuric jaundice, it is wiser to advise operation while the patient is in good health than to risk the serious complications already mentioned. We have no hesitation in offering this advice if the anæmia is in any way affecting the patient’s physical and mental health and causing a loss of efficiency. Additional reasons for advocating splenectomy are a past history of hæmolytic crises or a history of the disease occurring in a severe form in relatives, since it has been shown that the course of the disease runs fairly true to type

in different members of the same family. When the hæmolytic anæmia commences in infancy and early childhood, the dangers of biliary complications are remote for many years to come, and provided health is not impaired by anæmia, splenectomy may be safely postponed until the child is ten or twelve years of age, when the procedure is attended by less risk.

Should acute inflammation of the gall-bladder, necessitating laparotomy, occur in a patient with acholuric jaundice, it is generally advisable to limit the operative procedure to the gall-bladder and to undertake splenectomy at a subsequent suitable date. The interval between the operations should not, however, exceed a few months, since the excessive hæmolysis will continue until splenectomy is performed and, therefore, formation of calculi in the bile ducts may occur. On the other hand, if a chronically diseased gall-bladder with or without stones is found during an operation for splenectomy, the opportunity should then be taken to correct the biliary disease.

**Idiopathic Acquired Hæmolytic Anæmia.**—The so-called acquired form of acholuric jaundice in which the familial taint cannot be discovered occurs mainly in adult life and usually in a severer form. We have had two patients in whom a fall in the red cell count from approximately 5 to approximately 1 million occurred within twenty-four hours and was accompanied by severe epigastric pain, vomiting, collapse, and a temperature of 105° F. In cases of such severity blood transfusion must immediately be given and should be repeated several times if necessary. The dramatic improvement which frequently follows this form of therapy cannot be attributed only to the increase in oxygen-carrying capacity produced by the donor's red cells. There is evidence which suggests that some cases of acquired hæmolytic anæmia are due to the presence of a hæmolysin in the blood plasma or tissue cells, and since normal blood plasma has an antilytic action, the beneficial effects produced by blood transfusion may depend as much on the antilytic action of the transfused plasma as on the addition of the donor's red blood corpuscles to the patient's blood. Blood transfusion during hæmolytic crises has come, however, to be regarded as a potentially dangerous procedure, since it sometimes appears to precipitate an increase in the hæmolytic process. This effect is probably rare if the donor is of the same group as the recipient and if the transfusion is carried out slowly by the drip method. Universal donors should not be used for cases of hæmolytic anæmia unless the patient also belongs to Group IV (Moss); otherwise the donor's plasma may precipitate hæmolysis of the patient's red cells already being acted upon by autohæmolysins. Before, and for twenty-four hours after transfusion, 1 drachm (3·9 gm.) of bicarbonate of soda should be given every two hours, as by this means, should hæmolysis of the transfused cells occur, precipitation of hæmoglobin in the tubules of the kidneys, with the production of anuria, may be prevented or materially reduced. It should be noted, however, that recent investigations throw doubt on the value of alkalization in the prevention of anuria following intravascular hæmolysis.

In the majority of cases the results of blood transfusion are satisfactory as judged by improvement in the clinical condition of the patient, rise in the blood level and a reduction in the evidences of hæmolysis. A second or a third transfusion at intervals of a few days may be required to bring the patient to a suitable condition for the safe removal of the spleen. Un-

fortunately, blood transfusion is ineffective in a small proportion of cases, the gain in the blood level from the transfused corpuscles being more than counterbalanced by the excessive destruction of the patient's own cells. Should this be the case, emergency splenectomy, despite its obvious dangers, followed by another transfusion offers the only chance of saving life. The question of splenectomy in "acquired" hæmolytic anæmia is a vexed one. As many different types of hæmolytic disorders are embraced by this designation, it is desirable, before coming to a decision to operate, that an exhaustive investigation should be undertaken in each case by an expert hæmatologist to eliminate the Marchiafava-Micheli syndrome (nocturnal hæmoglobinuria) and hæmolytic anæmias secondary to morbid conditions such as Hodgkin's disease and carcinoma. A quarter of an hour before the splenic artery is tied, 0.5 c.c. of 1 : 1,000 solution of adrenaline should be injected subcutaneously, and after the artery has been tied an interval of three minutes should elapse before tying the splenic vein. As a result of these procedures we have found, from making blood counts at the operation, that a gain up to a million red cells per cubic millimetre of blood may result from the passage of erythrocytes from the congested spleen into the general circulation. When splenectomy has been satisfactorily accomplished in hæmolytic anæmias the principal source of blood destruction has been removed, although the fundamental defect in erythropoiesis remains unchanged. Since the bone-marrow is extremely hyperplastic, a rapid rise in the blood level occurs after splenectomy and a gain of  $\frac{1}{2}$  to 1 million cells per week may be confidently expected. The rapid rate of regeneration begins to slow down as the count approaches 3.5 to 4 million, and at this stage iron and whole liver are of value as hæmatinics. The general measures regarding rest, nursing, diet, etc., in a case of hæmolytic anæmia are identical with those required in any case of anæmia of similar severity and will be found on pp. 466-470.

#### SICKLE-CELL ANÆMIA

Sickle-cell anæmia, which occurs in negroes, is a very rare disease in this country. Treatment is purely symptomatic.

#### COOLEY'S OR MEDITERRANEAN ANÆMIA

This is a rare familial condition almost exclusively limited to children of southern European stock. The defect is believed to lie in the erythrocyte which is more resistant than normal to hypotonic saline. Although this trait is common, severe hæmolytic anæmia is exceptional. Splenectomy is ineffective, and treatment is purely symptomatic.

#### SECONDARY HÆMOLYTIC ANÆMIAS

The treatment of this group differs widely from that of primary hæmolytic anæmia, and consists not of splenectomy but of removing the causal condition together with attempts to relieve the anæmia by blood transfusions and hæmatinics. Accordingly, a suitable classification of the conditions producing a secondary hæmolytic anæmia facilitates an understanding of the problem.

## CLASSIFICATION

**Infections and Intoxications.**—Sepsis, streptococcal and staphylococcal septicæmia, gas gangrene (*clostridium welchii* infection), malaria, oroya fever.

In sepsis and in streptococcal and staphylococcal septicæmia it is now recognized that when severe anæmia develops it is, in most cases, due mainly to toxic inhibition of the bone-marrow, and that a direct hæmolytic action, resulting from the bacterial infection, plays only a minor rôle in the production of the anæmia. In gas gangrene, however, a severe anæmia may occur which is definitely due to increased hæmolysis.

**Drugs and Industrial Hazards:** *e.g.*, lead, phenyl-hydrazine, potassium chlorate, the arsenicals, arseniuretted hydrogen (particularly in submarine crews), dinitrobenzene (used in the manufacture of explosives), methyl chloride (used in domestic refrigerators), certain snake venoms. In view of the present wide use of sulphonamide preparations it is important to note that several cases of acute hæmolytic anæmia due to these drugs have been reported. This complication is so rare, however, that it should not be considered a contraindication to the employment of the drug in suitable cases.

**Occasionally in Other Diseases:** *e.g.*, Hodgkin's disease, syphilis, tuberculosis, reticulum-cell sarcoma, carcinomatosis, etc.

## TREATMENT OF SECONDARY HÆMOLYTIC ANÆMIAS

**Removal of the Cause.**—In infections this may mean the evacuation of local collections of pus, the administration of antibacterial or antitoxic sera, or the use of special drugs such as penicillin, the sulphonamides, quinine, or mepacrine. When the hæmolytic process is due to drugs, cessation of administration must be immediately ordered and, where possible, measures to increase elimination should be advised. If the poisoning is part of an industrial hazard, removal of the individual from the occupation is essential and the Inspector of Factories must be notified so that the hazard may be modified or eliminated by measures specially adopted to meet the circumstances. For details of the specific treatment of individual infections and poisoning with drugs and chemical substances, the reader is referred to the appropriate sections.

**Blood Transfusion.**—If the hæmolytic anæmia is chronic and mild to moderate in degree, blood transfusion is generally found to be unnecessary. On the other hand, if the infection is severe, the exposure to the poisonous substance is heavy, or idiosyncrasy is present to a marked degree, a rapid and severe hæmolysis may occur which will precipitate the patient into a state dangerous to life. In such cases, blood transfusion should be immediately given, and repeated if necessary. At the same time alkalis should be given orally, as described on p. 490, because of the danger of hæmoglobinuria and anuria.

**Hæmatinics.**—In all forms of secondary hæmolytic anæmia, iron, whole liver, yeast and dieto-therapy, as already described, should be ordered.

## PAROXYSMAL HÆMOGLOBINURIA

Hæmoglobinuria results from an intravascular hæmolysis sufficient to raise the plasma hæmoglobin above the renal threshold. Accordingly it may occur in any type of anæmia resulting from intravascular hæmolysis. The following types are usually accepted as distinct clinical entities.

*Cold Hæmoglobinuria.*—In this type, rapid hæmolysis leading to hæmoglobinæmia and hæmoglobinuria occurs when the patient enters a warm atmosphere after having been exposed to cold. In such cases there is an abnormal lysin in the patient's serum. Preliminary cooling is essential for the union of lysin and red cells and the action of complement occurs when the body is subsequently warmed. Syphilis is the principal ætiological factor. The condition can be recognized by the Donath-Landsteiner test.

**Treatment.**—Prophylaxis, which should include avoidance of all forms of chilling, *e.g.*, washing the hands in cold water or drinking cold fluids, is an important part of the treatment.

Thorough and prolonged antisymphilitic treatment should be instituted, and it is claimed by some authorities that this is usually successful and may cause disappearance of the autohæmolysin from the blood.

During an attack the body should be kept warm and alkalis (see p. 490) and plenty of fluids should be given by mouth. If anæmia results, iron therapy (see p. 470) should be instituted. These measures are equally applicable to all types of hæmoglobinuria.

*Hæmoglobinuria on Exertion.*—This type occurs in young males and is probably analogous to postural albuminuria.

**Treatment.**—Usually no treatment is necessary since it is a mild disease which disappears when adult life is reached.

*Nocturnal Hæmoglobinuria* (Marchiafava-Micheli syndrome).—Ætiology is obscure although recent work suggests that it is due to an inherent defect of the red cell which renders it susceptible to lysis when a slight lowering of the hydrogen-ion concentration of the blood occurs consequent on reduced pulmonary ventilation during sleep.

**Treatment.**—Treatment is unsatisfactory and is mainly symptomatic. Splenectomy is contraindicated. For the severe hæmolytic crises small transfusions of 250 to 500 c.c. of carefully matched blood, given very slowly, are indicated. Severe reactions, however, are liable to occur.

## FABISMUS

Fabismus is the name given to a hæmolytic anæmia accompanied by severe hæmoglobinuria which is essentially confined to southern Europe, particularly Italy and Sardinia. It is believed to result from the ingestion of the bean, *vicia faba*, or inhalation from the bean plants which are grown in abundance in the localities concerned.

**Treatment.**—Treatment consists in avoidance of the bean together with symptomatic measures for the hæmolytic anæmia when required.

## BLACKWATER FEVER AND POST-TRANSFUSIONAL HÆMOGLOBINURIA

(See pp. 244, 942.)

## THE ACUTE HÆMOLYTIC ANÆMIA OF LEDERER

Since the ætiology is obscure, this form of anæmia is considered separately. The presence of leucocytosis, high fever and anæmia has led many authorities to suggest that the hæmolytic process is due to an unknown infective agent, a view with which we are unable to agree since identical manifestations are found in any severe hæmolytic anæmia.

**Treatment.**—The treatment to be adopted is blood transfusion, which should be repeated if recovery does not rapidly occur. Beneficial effects may result from blood transfusion in any type of hæmolytic anæmia, but the rapid and lasting improvement which occurs in Lederer's anæmia appears to be much more marked than in other hæmolytic anæmias. Indeed, it is mainly this characteristic which has been responsible for the description of Lederer's anæmia as a separate entity.

The general measures described regarding nursing, diet, and hæmatinics on pp. 466-470 are equally necessary in this condition.

## APLASTIC AND HYPOPLASTIC ANÆMIA

Aplastic and hypoplastic anæmias result from a loss, complete or partial, of the erythroblastic, leukoblastic, and thromboblastic cells in the bone-marrow.

In certain cases, especially when the disease occurs in an acute form in young persons, the cause is unknown and the name "idiopathic or primary aplastic anæmia" is used, while in others—the disease may occur at any age—it is usually more chronic and is frequently secondary to some recognizable infective or toxic element.

Accordingly, it is desirable to have a clear conception of the causes known to produce an aplastic or hypoplastic state of the bone-marrow.

### CAUSES OF SECONDARY APLASTIC OR HYPOPLASTIC ANÆMIA

#### *Drugs and Physical Agents.*

- (a) The heavy metals. Gold, mercury, silver, bismuth, arsenic, lead.
- (b) The benzol compounds. Benzol, trinitrotoluol, dinitrophenol, etc.
- (c) Poisonous gases. Carbon monoxide, methane, mustard gas.
- (d) Radio-active materials and X-rays. Radium, radon gas, thorium.

#### *Hazardous Occupations.*

- (a) Benzol. In the following occupations benzol is used for its solvent properties: rubber workers, dry cleaners, tanners, varnish and paint workers, gilders, feather workers, milliners, printers and tanners.
- (b) Lead. Painters, plumbers, etc.
- (c) Trinitrotoluol. Munition workers.
- (d) Gases. Soldiers, sewer workers, mine workers.
- (e) Radio-active substances. Luminous-paint workers, workers with X-rays and radium.

**Infections and Intoxications.**—While aplasia is rare, hypoplasia of the bone-marrow not infrequently results from infections and intoxications. Occasionally, particularly in children, inhibition of the bone-marrow may rapidly result if the infective process is extremely severe, as may occur in typhoid fever, diphtheria, miliary tuberculosis, malignant endocarditis, influenza and pneumonia. More usually, a hypoplasia occurs insidiously and as the result of long-continued chronic infections, such as chronic pulmonary tuberculosis, osteomyelitis, rheumatic fever, malaria and other chronic tropical diseases. The relationship of hypoplasia of the bone-marrow to focal sepsis (in teeth, tonsils, appendix and gall-bladder) is far from clear.

In some cases no improvement of the blood picture occurs until the focus of infection has been removed, while in others this procedure effects no beneficial change, thus suggesting that the focus of infection was the result rather than the cause of the anæmia. Accordingly, wide experience and sound judgment are required in making a decision as to when and whether foci of infection should be removed, in view of the particular dangers associated with this procedure in the presence of aplasia and hypoplasia of the bone-marrow.

*Terminal States of Certain Diseases.*—The bone-marrow becomes progressively exhausted towards the termination of many diseases of long standing. This is particularly true of the blood diseases, such as pernicious anæmia, pellagra, leukæmia, erythræmia, myelophthisic anæmia and rarely in chronic post-hæmorrhagic anæmia, but it also may occur in diseases of the endocrine glands such as myxœdema or as the result of severe and long-continued deficiency of nutritional factors, both vitamin and mineral, essential to health.

Lastly, bone-marrow inhibition may be very severe in the terminal stages of hepatic and renal failure, especially in chronic kidney disease with nitrogen retention, in which a progressive anæmia develops which is little influenced by liver or iron.

A study of the list submitted above of factors which can cause aplasia or hypoplasia of the bone-marrow might lead one to suppose that severe types of anæmia from these causes are of frequent occurrence. In actual practice, however, aplastic anæmia, whether primary or secondary, is extremely rare, although mild degrees of bone-marrow inhibition are not uncommon. Since only a small minority of individuals exposed to risk actually suffer from aplastic anæmia, an unexplained idiosyncrasy of that individual's bone-marrow to toxic and infective processes is probably the most important factor in its production, as is also evidenced by the fact that the severity of the anæmia may bear no relationship to the dosage of the toxic agent. However, it is a sound rule to remember which drugs have this peculiar selective action on the formative tissues and to be on the outlook for such changes by recognition of the early clinical symptoms (purpura, sepsis and exhaustion) and changes in the blood (anæmia, leucopenia and thrombocytopenia).

**Treatment.**—In all cases of aplastic and hypoplastic anæmia, the patient should be confined to bed and the general measures suitable for the degree of anæmia, as outlined on p. 466, instituted.

Where the blood level is so low as to endanger life (see p. 479), blood transfusion should be undertaken at once and repeated at intervals as required in order to keep the blood at a level at which the patient is free from risk to life. At the same time iron, yeast and whole liver or proteolyzed liver by mouth and liver extract by injection should be given. In our experience folic acid is ineffective in aplastic anæmia. Since improvement has been reported in a few cases by other writers, it is justifiable to prescribe folic acid (20 mg. daily) provided the test period is limited to three weeks. By these means symptomatic relief may be given and time is secured to enable the physician to search for and if possible remove the causal factor.

A consideration of our classification of the ætiological factors as outlined above will indicate the investigations and treatment required in individual cases.



Where no obvious cause can be found other than the presence of focal sepsis in the teeth, tonsils, sinuses, etc., it is wise to try the effects of rest, diet, hæmatinics and blood transfusions before resorting to the removal of the focus in the hope that improvement in the local condition may occur concomitantly with the raising of the patient's resistance and the improvement in the anæmia resulting from the general measures described.

Should the patient continue to go downhill, however, it may be necessary to eradicate such foci despite the recognized danger of resultant sepsis, necrosis and hæmorrhage at the site of the operation. This danger is obviously connected with the failure in production of leucocytes and thrombocytes, whose function is to control infection and bleeding.

The minimal amount of operative interference should be undertaken at one time and should generally be preceded and followed by a blood transfusion and the administration of penicillin.

If a diagnosis of idiopathic aplastic anæmia is made because at the end of some weeks the patient's condition and the blood picture continue to deteriorate and the fullest investigation fails to produce any evidence of any causal condition, or if a cause is discovered which is found to be irremediable, blood transfusions should be discontinued and the patient allowed to die under the influence of morphia.

In cases of hypoplasia of the bone-marrow for which no cause can be found and in cases of aplasia or hypoplasia where a cause is discovered which can be removed, the patient should be kept alive with blood transfusions and the other remedies mentioned should be continued, if necessary, for months or even years, in the hope that bone-marrow regeneration will occur in the interval. The method of drip transfusion is particularly valuable, because by this means a massive transfusion of 3,000 to 4,000 c.c. of blood may be given over forty-eight hours and may maintain a satisfactory blood level for several months thereafter.

## SPLenic ANÆMIA

Splenic anæmia (Banti's disease) is more a syndrome than a disease and in its commonest form may be described as a chronic condition characterized by splenomegaly and hypochromic anæmia with leucopenia, no enlargement of lymphatic glands, a tendency to hæmorrhage from the alimentary tract, and, in the late stages, a liability to cirrhosis of the liver.

Before the diagnosis of splenic anæmia is accepted the following conditions, in which anæmia and splenomegaly occur, must be eliminated:—

1. Acute and chronic infectious diseases with splenomegaly, *e.g.*, infective endocarditis, malaria, schistosomiasis, kala-azar and syphilis.
2. Pernicious anæmia (see p. 479).
3. The hæmolytic anæmias (see p. 488).
4. Idiopathic thrombocytopenic purpura (see p. 505).
5. Chronic nutritional hypochromic anæmia (see p. 464).
6. The reticuloses, including the leukæmias (see p. 517).

When this is done a residue of cases is left, in some of which the splenomegaly has obviously occurred secondary to cirrhosis of the liver, whereas, in others, enlargement develops apparently prior to the disease of the liver.

The name "Splenic Anæmia" should be confined to this latter group, which forms the subject of this section.

Treatment will be considered under two headings:—

1. Operative measures, including splenectomy.
2. Symptomatic treatment.
  - (a) Diet and iron.
  - (b) Blood transfusion.

**Operative Measures.**—Splenectomy is the operation which is most generally undertaken.

Since the rationale of splenectomy as a form of specific treatment in splenic anæmia was based mainly on the assumption that the spleen is the primary locus of the causal factor, it is necessary to consider this hypothesis further.

The principal evidence advanced by the supporters of this hypothesis is the occurrence of splenomegaly for a considerable time before the development of cirrhosis of the liver, as judged by the presence of the accepted clinical manifestations of this condition, and the normal histological appearances present in biopsy specimens in a proportion of cases.

The reasons for not accepting this hypothesis may be summarized as follows:—

1. The histological picture of the spleen is that of long-standing passive congestion and is identical with the pathological features found in the spleen in cases of primary cirrhosis of the liver, and hence is in keeping with the hypothesis that the splenic changes are secondary to portal obstruction.
2. The presence of greatly dilated veins in which an increased pressure can be demonstrated by direct measurement clearly indicates the existence of obstruction to the portal vein or its radicles.
3. The absence of pathological changes in the liver in many cases of splenic anæmia can be explained by the block in the portal circulation being extrahepatic in situation.
4. Cirrhosis of the liver may progress and hæmorrhages from the stomach and œsophagus recur, or even start for the first time, subsequent to removal of the spleen.

Accordingly, we are unable to agree that there is any satisfactory evidence in favour of the hypothesis that the disease starts primarily in the spleen and suggest that the consensus of modern opinion supports the view that the splenomegaly is secondary to portal hypertension.

Moreover, there is little evidence that the anæmia in splenic anæmia is due to blood destruction. Hence the beneficial effects claimed for splenectomy must rest mainly on anatomical and mechanical foundations.

Until recently the importance of these factors was not fully understood or appreciated, and this explains the wide divergence of opinion which exists in regard to the value of surgery in the treatment of splenic anæmia, the types of operation advised and the results achieved.

In patients with splenic anæmia the advisability of surgical treatment must be based on an assessment of the amount, type and site of obstruction to the portal circulation. The obstruction may be intrahepatic or extrahepatic in site. Cirrhosis of the liver, especially of the Lænnec type, is the principal cause of intrahepatic obstruction. Cavernous transformation or

thrombosis of the portal vein or its main tributaries due to inflammation, trauma or pressure from without are the main causes of extrahepatic obstruction. In the latter group the hepatic parenchyma usually shows little or no pathological change. Surgical treatment offers the only hope of reducing the portal hypertension and hence decreasing the liability to gastro-intestinal bleeding. In addition it may possibly retard the progress of pre-existing hepatic disease by improving the delivery of oxygen to the liver via the hepatic artery consequent on a reduction of congestion of the liver sinusoids. The clinical history and physical examination, together with the assessment of liver function by special tests including biopsy, play an essential part in deciding on the advisability of operation and the most suitable surgical procedure. If advanced liver cirrhosis is present and the patient's clinical state is poor, operative interference is contraindicated. If the assessment of the case indicates that pathological changes in the liver are only moderate, slight or absent, while the dangers of hæmorrhage from œsophageal or other varices are great, operation should be undertaken. The details are decided by the findings after the abdomen has been entered. If the portal hypertension is due to intrahepatic block or to extrahepatic block in the portal vein, splenectomy and left nephrectomy should be undertaken and the splenic vein anastomosed to the left renal vein; or the portal vein is anastomosed to the inferior vena cava. These operations have been successfully carried out in America and in Edinburgh. They should be undertaken only by surgeons of wide experience and with a special knowledge of the technique of blood-vessel surgery. Several years must elapse before a proper assessment of these operative procedures can be made. For further information the reader is referred to the paper by A. O. Whipple (*Annals of Surgery*, 1945, **122**, 449). When the block is extrahepatic and in the splenic vein, splenectomy alone will cure the syndrome since the liver is undamaged and the danger of hæmorrhage is removed. Whipple states that splenic vein obstruction is much less common than portal vein obstruction. In the last two cases of splenic anæmia under the senior author's care in which splenectomy was undertaken because of severe repeated gastro-intestinal bleeding, the block was found in the splenic vein, the liver was normal, and complete cure is confidently expected. Other operative procedures which have been undertaken with the object of reducing the incidence of hæmatemesis are ligation of the coronary vein of the stomach and the production of a collateral circulation in the abdomen through post-operative adhesions (omento-pexy, Talma-Morrison operation). The results achieved are uncertain and usually unsatisfactory. Treatment aimed at thrombosing dilated œsophageal veins by injecting them through an œsophagoscope with sclerosing solutions such as are used in the treatment of varicose veins of the legs, has been undertaken in a limited number of cases. Our experience of this ingenious but potentially dangerous procedure does not lead us to recommend it.

Irradiation of the spleen is of no curative value in splenic anæmia but may cause a diminution in the size of the organ, thereby relieving abdominal discomfort.

**Symptomatic Treatment.**—The general treatment of the anæmia in splenic anæmia is on the lines indicated on pp. 466-470. When a large hæmatemesis occurs, the patient is suffering from acute post-hæmorrhagic anæmia, for the treatment of which see p. 474. In other cases a chronic

hypochromic anæmia results from continuous occult bleeding from the gastric and œsophageal varices, and the measures outlined on p. 476 will be found to be suitable.

*Diet.*—A diet should be prescribed rich in the food factors valuable for blood formation, in particular, liver, kidney and butcher meat. Indigestible articles of food which are liable to injure mechanically the gastric and œsophageal varices should be excluded from the diet or their irritating components removed. The following articles should be excluded—highly seasoned and indigestible foods, condiments and pickles, the skins and pips of fruits, nuts, etc.—and coarse vegetables and fruits should be passed through a sieve and served as purées or fools.

*Iron.*—A study of the best-known textbooks of medicine suggests that iron is of little or no value in the treatment of splenic anæmia. Our experience of the excellent results which may frequently be obtained leads us to protest against this view. We have obtained rapid rises in the hæmoglobin level when iron was given in the preparations and doses stated on p. 470. It is only in the late stages of the disease, when hepatic failure is approaching, that iron therapy begins to fail.

*Blood Transfusion* is of great value in the treatment of the shock following the severe hæmorrhages which occur in splenic anæmia. By this means we have repeatedly tided patients over emergencies and prolonged life for years. Iron therapy should be started immediately after the transfusion. Blood transfusions should be discontinued only when there is clear evidence that an advanced stage of liver failure has been reached or when hæmorrhages are recurring at short intervals and operative procedures to relieve the portal hypertension cannot be undertaken. At this stage of the disease the patient is living on top of a volcano and the mental misery entailed by the constant fear of another hæmatemesis is of such a degree that it makes it inadvisable to attempt to prolong life.

For the treatment of cirrhosis of the liver, ascites and hæmatemesis, see pp. 589-592.

## POLYCYTHÆMIA VERA

(*Erythræmia*; *Splenomegalic polycythæmia*; *Vaquez's disease*; *Osler's disease*)

A rare disease characterized by polycythæmia, increased viscosity and blood volume, and by cyanosis and splenomegaly.

An increase of red cells may be absolute or relative. An example of the latter is the polycythæmia secondary to diminution of the fluid part of the blood, consequent on severe sweating, vomiting, or diarrhœa. Another example is the high red cell count found in individuals with chilblains and Raynaud's disease when blood is taken from an area of local congestion. Capillary stasis causes concentration of the blood in the affected areas. An absolute increase of red cells results from one of two causes: (1) a primary disease of the erythroblastic tissues, analogous to the hyperplasia of the leucoblastic tissues in leukæmia—hence the name "erythræmia"; and (2) a compensatory hyperplasia of the erythron secondary to factors which lead to incomplete oxygenation of the blood. The term "erythrocytosis" should be confined to this type of polycythæmia. The conditions predisposing to erythrocytosis are chronic cardiac and pulmonary disease, either congenital or acquired, living at high altitudes and the toxic effects of

various poisons, *e.g.*, carbon monoxide, phosphorus, aniline dyes, etc. A diagnosis of polycythæmia vera should never be made till the more common conditions which cause erythrocytosis have been excluded.

**Treatment.**—Since the clinical manifestations of polycythæmia vera are directly attributable to increased blood volume and increased blood viscosity, treatment must be directed to the relief of these features by reducing the number of red blood cells in the circulation. For this purpose many different methods have been employed, most of which have proved ineffective. Splenectomy is contraindicated. Benzol should not be used because of its excessively toxic and depressant effect on the bone-marrow. Arsenic in large doses (see p. 519) may be of some value and may be tried, should the forms of treatment recommended below fail. The claims regarding the value of splenic extract therapy have not been confirmed. The claim that a marked reduction in the intake of foods rich in the extrinsic factor of Castle (see p. 478) will reduce the activity of the bone-marrow in polycythæmia vera has not been substantiated. Such a diet is contraindicated in a chronic disease lasting many years. However, a moderate reduction in animal protein and the prohibition of foods rich in purines (liver, kidney, sweetbread, etc.) may be recommended when a raised blood pressure and its sequels have developed in polycythæmia.

The physician has the choice of three main methods of treatment: (1) venesection; (2) irradiation with X-rays or radium; and (3) phenylhydrazine or its derivative acetylphenylhydrazine. A combination of these methods may be used.

**Venesection.**—To be of any value a large quantity of blood must be withdrawn, since the blood volume is often increased two or three fold. Little relief is likely to follow the withdrawal of less than 40 oz. There can be no doubt that venesection gives more rapid relief from subjective symptoms than any other form of treatment. Its effect is, however, transitory, and it should not be used as the sole method of treatment. In an acute exacerbation of subjective symptoms, particularly if they suggest a liability to intracranial hæmorrhage or thrombosis, it is the method of choice.

Owing to the greatly increased viscosity of the blood, venesection is unlikely to be successfully accomplished unless certain modifications of the usual methods are employed.

1. A thick-bore French's needle should be used and the rubber connection attached to this and leading to the receptacle for the blood should be as short as is consistent with convenience and thoroughly washed with sodium-citrate solution before use.

2. When the vein has been selected, the needle should be inserted in the direction opposite to that of the blood stream.

3. A vacuum should be maintained in the blood receptacle to hasten the rate of blood flow through the tubing, and so prevent clotting.

**Irradiation.**—The idea of applying "stimulating" doses of X-rays to the spleen with a view to increasing the activity of the reticulo-endothelial system has now been abandoned in favour of depressant doses applied according to the method described on p. 521. It is probable that cases with a high platelet count are particularly suitable for irradiation therapy rather than for phenylhydrazine treatment, since in such cases the tendency to thrombosis, already present, will be increased by treatment with the drug.

*Radio-active Phosphorus* has been used in America for the treatment of polycythæmia vera. The methods employed are similar to those used for the treatment of leukæmia (see p. 518). The results obtained in a series of ninety cases treated at one American clinic between 1939 and 1947 are most impressive. The risks are similar to those occurring with X-ray treatment unless dosage is carefully controlled in each individual patient. Radio-active phosphorus is not available for therapeutic purposes in Great Britain at time of writing.

*Phenylhydrazine Hydrochloride*.—The effects of this drug have been carefully investigated by Giffin and Allen, who claim that in thirteen out of fifteen cases fairly good, good or excellent results were obtained. The following features are held to contraindicate treatment with phenylhydrazine: (1) age over sixty; (2) advanced arteriosclerosis; (3) bedridden cases; (4) cases with a history of thrombosis; (5) cases with definite disease of the liver or kidneys. It is essential that the drug should be freshly prepared. In the initial period of treatment, patients should be in hospital so that proper supervision may be carried out, but they should be ambulatory and may, in some cases, receive a course of massage in order to lessen the susceptibility to thrombosis. Dosage: 0.1 gm. in capsule two or three times a day until 3 to 4 gm. are given, or until definite clinical evidence of active hæmolysis (jaundice) occurs. The initial treatment usually lasts from ten to fourteen days. The drug should then be stopped, as the effect is cumulative and lasts for seven to ten days after its withdrawal. In cases which prove resistant, one or more courses of treatment with the drug (0.1 gm. b.i.d., for five days) may be given at intervals of ten days. Maintenance treatment should be commenced within a few weeks of the initial course. The amount necessary for maintenance of a blood count at more or less normal levels has to be found by trial and error in each individual case; a dose of from 0.1 to 0.3 gm. on one day of each week is the average amount necessary. Long-continued treatment of this kind may occasionally be followed by a complete remission of the polycythæmic process for long periods. Thrombosis appears to be the main danger, while gastro-intestinal disturbances may cause some difficulty in administering the drug.

*Acetylphenylhydrazine*.—This has been recommended by Stone, Harris and Bodansky, and by Rosenthal. It is preferred to phenylhydrazine on the following grounds: it is practically as effective, it is less toxic and the dosage is more readily controlled. Dosage: 0.1 gm. once daily in a gelatin capsule, for one or more courses of seven to ten days, during which the red cell count should be carefully watched. For maintenance purposes the dose is approximately 0.1 gm. at intervals of five to seven days. Rosenthal found large amounts necessary in cases with initially high counts (about 10,000,000), e.g., 0.1 gm. daily for three to five weeks.

*Conclusions*.—For an emergency, venesection should be employed. Irradiation appears to be of more general application than treatment with phenylhydrazine, since many cases are not suitable for treatment with the drug. Our recent experiences with X-ray therapy have been so satisfactory that we feel that it is the method of choice. A combination of phenylhydrazine and irradiation is recommended by Rosenthal for the leukæmoid group of cases.

*Symptomatic Treatment*.—A patient with polycythæmia may complain of a variety of symptoms which are principally referable to the nervous,

gastro-intestinal and cardiovascular systems. Since they are all due to the high blood volume and increased viscosity of the blood, the measures outlined above to correct these conditions are themselves the best form of symptomatic treatment. The administration of sedative drugs to control the insomnia, giddiness and psychic disorders which are so frequently present may, however, be needed (aspirin, phenacetin, bromides, chloral and the barbiturates). For dyspepsia, a light easily digested diet together with alkalis is advised. Constipation should be treated as outlined on p. 467. Purging with salines should be avoided as this will still further concentrate the blood.

The occurrence of hæmorrhage indicates that nature is attempting to relieve the plethora and no treatment should be undertaken to stop it unless excessive quantities of blood are lost. The liability to thrombosis is best reduced by controlled irradiation therapy and by prescribing regular exercise to maintain an active circulation. Some authorities recommend the administration of 30 to 60 gr. (1.8 to 3.6 gm.) of potassium citrate four times a day, particularly during the time when phenylhydrazine is being administered.

## ENTEROGENOUS CYANOSIS

(*Methæmoglobinæmia; Sulphæmoglobinæmia*)

A disease characterized by chronic cyanosis due to the presence of methæmoglobin, or sulphæmoglobin, in the circulating blood.

**Prophylaxis.**—In the great majority of cases the condition is caused by the ingestion of drugs, *e.g.*, phenacetin, acetanilide, nitrites, sulphonal, potassium chlorate and trional, and recently much attention has been drawn to its frequent occurrence during the administration of the sulphonamide group. The outstanding characteristic of the condition is the presence of cyanosis without accompanying cardiac or pulmonary lesions, and, usually, without respiratory distress. Methæmoglobinæmia is due to a direct chemical action of one of the drugs mentioned on the hæmoglobin of the circulating erythrocytes, and it rapidly disappears after removal of the causative agent. Sulphæmoglobinæmia, which is much more serious and persists for several weeks after cessation of the drug, is caused by a sensitization of the red cells which results in a combination between their contained hæmoglobin and hydrogen sulphide absorbed from the intestine. The differentiation between the two conditions is made by spectroscopic examination of the blood. The occurrence of sulphæmoglobinæmia may be prevented in a large proportion of cases by correcting constipation before prescribing any of the drugs mentioned. During their administration regular bowel evacuations should be produced by liquid paraffin and occasional enemas rather than by laxatives or purgatives, particularly magnesium sulphate, which renders the contents of the colon fluid and so increases the formation of hydrogen sulphide.

**Curative Treatment.**—The alarming appearance of the patient is in striking contrast to the absence of any distress and, usually, no treatment is required other than withdrawal of the causative drug.

If the concentration of methæmoglobin is high, symptoms due to anoxæmia may occur, particularly if the condition supervenes in a disease which by itself causes some degree of anoxæmia. For example, methæmo-

globinæmia may intensify considerably the anoxæmia in lobar pneumonia and in anæmia. In such cases oxygen inhalation is indicated and treatment with methylene blue should be instituted. This drug in a dosage of 1 to 2 gr. (0.06 to 0.12 gm.) six times daily by mouth is effective within a few hours. In the rare critical cases where even such a short delay would be dangerous, 10 to 20 c.c. of a 1 per cent. aqueous solution should be given intravenously (care being taken to avoid injection into the subcutaneous tissue) and oral administration begun at the same time.

Recent work on familial idiopathic methæmoglobinæmia has demonstrated the value of large doses of ascorbic acid in this rare condition. The question therefore arises whether ascorbic acid may be of value in other forms of methæmoglobinæmia.

Sulphæmoglobinæmia may produce respiratory embarrassment in patients who were severely anæmic before the onset of the condition, and in whom, therefore, the further reduction of hæmoglobin capable of combining with oxygen results in the symptoms of anoxæmia. In such cases blood transfusions should be given at intervals to relieve respiratory distress until reduction of the sulphæmoglobinæmia and increase in the blood level following appropriate anti-anæmia therapy produce a hæmoglobin level sufficient for the needs of the body. Methylene blue is ineffective in sulphæmoglobinæmia.

## THE HÆMORRHAGIC DISEASES

The group of diseases dealt with in this section comprises diverse pathological conditions affecting the capillaries, the platelets and the factors concerned with blood coagulation. Hæmorrhage into the skin and mucous membranes is a clinical feature common to all. The control of hæmorrhage due to trauma or other diseases is not considered here. The following classification is proposed as a useful working basis for the practitioner.

### A. Defects in the Clotting Mechanism.

1. Hæmophilia (hereditary thromboplastinopenia).
2. Hypoprothrombinæmia, which occurs in
  - (a) hæmorrhagic disease of the newborn;
  - (b) biliary obstruction and intestinal disorders such as sprue and ulcerative colitis;
  - (c) severe hepatic damage.
3. Fibrinopenia.

### B. Defects in or Damage to the Capillaries.

Due to:—

- (a) *Infections* (usually severe in degree and particularly if a septicæmia is present) with streptococcus hæmolyticus and viridans, meningococcus, *B. typhosus*, *B. diphtheriæ*, *B. tuberculosis* (especially in miliary forms) and the viruses of typhus fever, measles, smallpox, etc.
- (b) *Drug Intoxications*, e.g., sulphonamides, benzol, organic arsenicals, quinine, aniline dyes, ergot, sedormid, gold, bismuth, mercury, iodides (for industrial hazards connected with these, see p. 494).



- (c) *Chronic Diseases* of kidneys and liver, malignant disease and, rarely, in the terminal stage of chronic cardiovascular disease.
- (d) *Avitaminosis*—scurvy.
- (e) *Allergic states*, including Schönlein's and Henoch's purpura.
- (f) *Congenital Defects*—hereditary telangiectasis; hereditary familial purpura.

C. *Defective Production or Excessive Destruction of Platelets.*

- 1. Primary: idiopathic thrombocytopenic purpura.
- 2. Secondary: due to
  - (a) *Exposure to X-rays* or radio-active substances.
  - (b) *The Terminal States of Blood Diseases*—aplastic anæmia, pernicious anæmia, the leukæmias, hæmolytic anæmia, splenic anæmia, Gaucher's disease.
  - (c) *Primary and Secondary Malignant Disease* of bones and bone-marrow, and osteosclerosis.
  - (d) *Severe infections and intoxications* which may damage the bone-marrow in addition to the capillaries.

It should be pointed out that there is no general unanimity of opinion concerning the mechanism underlying the bleeding tendency in thrombocytopenic purpura. While the deficiency of platelets provides the simplest and most obvious explanation, some authorities hold that the primary fault lies in the capillaries.

#### METHODS FOR THE CONTROL OF BLEEDING

In the hæmorrhagic diseases, in which the bleeding tendency may be caused by such widely differing factors as capillary permeability, platelet deficiency or intrinsic defects in the clotting mechanism, it is important that correct diagnosis should precede treatment. Nevertheless, in practice it is found that pressure augmented by the local application of certain blood coagulants, together with the transfusion of whole blood, have a general field of usefulness. This statement in no way removes the necessity for making a careful search in every case of hæmorrhage for a possible cause and the institution of measures for its removal or neutralization where possible. A study of the list of causal conditions given above will suggest the type of treatment indicated in individual cases. A full blood examination is essential to eliminate the primary blood diseases in which purpura occurs, to assess the degree of anæmia present, and to establish whether the purpura is of the thrombocytopenic or non-thrombocytopenic variety.

#### THE PURPURAS

Purpura is a symptom rather than a disease, and the term is used to describe a condition in which extravascular hæmorrhage occurs in the skin and subcutaneous tissues, from the mucous membranes and rarely in serous cavities. In this section the term "purpura" is restricted to the hæmorrhagic states resulting from, platelet deficiency or capillary damage from

whatever cause, but does not include the diseases resulting from intrinsic defects in the clotting mechanism, *e.g.*, hæmophilia, hypoprothrombinæmia and fibrinopenia.

The purpuras are best divided into two groups:—

*Primary* or Idiopathic—in which no cause can be found.

*Secondary* or Symptomatic—in which the symptom-complex is due to a recognizable cause.

Both primary and secondary purpuras may be thrombocytopenic or non-thrombocytopenic. Since a search for a cause must be undertaken in every case, the classification given on pp. 503-504 will be found to be of value in helping the practitioner to discover the ætiological factor.

The treatment prescribed should be based mainly on the severity of the hæmorrhagic state, and the cases can generally be classified into three groups:—

### I. MILD PURPURA

Where the escape of blood into the skin or from the mucous membranes is small in extent and does not by itself produce incapacity. Thus, a few purpuric spots not infrequently appear during the course of the exanthemata or in children without any obvious cause. This condition is referred to in many textbooks as purpura simplex. On the other hand, a mild degree of purpura may appear in the late stage of very serious diseases such as chronic nephritis, malignant disease and the leukæmias. In both types of case no particular treatment for the purpura itself is required.

### II. PURPURA OF MODERATE SEVERITY

Where the purpura is sufficiently severe to lead to anæmia and general systemic disturbance. In this group, hæmorrhages from the mucous membranes, particularly nose, gums, alimentary tract and uterus, are of importance.

Treatment is considered under the headings of local and general measures.

**Local Measures.**—*Bleeding from the Gums.*—The most effective preparation for the local control of hæmorrhage is Russell's viper venom, which is an extremely powerful coagulant having the additional advantages that it does not injure the tissues and that it acts efficiently even in very low dilutions. It is supplied under the name of Stypven by Messrs. Burroughs Wellcome & Co., and as Rusven by Boots Pure Drug Co. Since the efficacy of solutions of the venom decreases rapidly, the venom in dry form and sterile distilled water are supplied in separate ampoules and the solution is prepared by dissolving the powder in the distilled water immediately before use. The site of bleeding should be thoroughly cleaned and all friable clots removed. A gauze dressing soaked in the venom solution is then applied firmly but without undue pressure. Different contrivances according to the site of the bleeding area may be necessary to keep the dressing in position; for example, a well-fitting dental plate may solve this problem admirably and so avoid the repeated application of fresh dressings which is necessary if they are easily displaced by movements of the tongue.

According to Macfarlane, the dressing is more effective if the solution is first heated to 50° C., and, if the bleeding is very intractable, an equal mixture of the venom solution and 1 : 1,000 solution of adrenaline may be tried as a last resort. If Stypven is not available, gauze soaked in normal fresh human blood should be applied to the site after it has been properly cleaned. It is important to bear in mind that excessive pressure to the site of hæmorrhage may control the bleeding temporarily, but may cause such devitalization of the tissues that necrosis and sloughing occur, with hæmorrhage from a larger area than the initial one.

The effects produced by the measures described above are much superior to those obtained by the use of acids, iron salts, collodion, gelatin, the various commercial hæmostatic sera and tissue extracts, and cauterization of the bleeding area by direct heat or diathermy.

*Bleeding from Tooth Sockets.*—A frequent source of intractable hæmorrhage, particularly in hæmophilics, is the socket left after the extraction of a tooth. Local anæsthesia with adrenaline should not be used. The wound should be thoroughly cleaned and a gauze plug soaked in Stypven solution inserted. Pressure should be applied in such a way as to compress the wound surfaces together rather than to splay them apart as happens when a pledget of cotton-wool is pressed into the socket. If there is no infection this treatment is likely to be rapidly successful. Where gross infection of the socket coexists it is obviously undesirable to close the wound completely, and one should be satisfied with light plugging which will allow drainage. In such cases a certain amount of hæmorrhage is unavoidable. When a marked hæmorrhagic tendency is present it is seldom advisable to attempt to reduce hæmorrhage from a tooth socket by the insertion of sutures, since these "cut out" frequently and defeat their purpose by increasing the bleeding area.

*Bleeding from the Nose.*—The control of epistaxis is dealt with on p. 699.

*Oral Sepsis.*—Oral sepsis frequently complicates hæmorrhagic lesions of the mouth, especially in the leukæmias. Since spirochætes are almost invariably present in these lesions it has been customary to apply a neoarsphenamine paint (0.9 gm. to 9 c.c. glycerin and 9 c.c. water) to the affected area, or to give 0.3 gm. neoarsphenamine intravenously at intervals of three or four days. This use of mouth-washes and arsenic has been largely replaced by local penicillin therapy (see p. 93), which has been shown to be particularly effective for the treatment of streptococcal and spirochætal lesions of the mouth and throat.

*Absorbable Hæmostatics.*—Intensive research during the late war produced a new series of hæmostatics which could be applied locally and which are spontaneously absorbed in a period of days or weeks. These preparations can be divided into two main groups, namely (1) those derived from plasma, and (2) those from other sources. The former group consists of such preparations as fibrinogen, fibrin or thrombin, which are applied to the bleeding surface singly or in combination. The second group includes oxidized cellulose, gelatin sponge and calcium alginate derived from seaweed. The hæmostatic effect of all these preparations is probably related to the great surface which they offer to extravasated blood. The plasma preparations have in addition a direct effect on blood coagulation. These new hæmostatic agents have been widely and successfully used by surgeons, and particularly neuro-surgeons, in America. Their value in medical diseases

characterized by the bleeding tendency, such as thrombocytopenic purpura and hæmophilia, awaits further investigation.

*Conclusion.*—Although the measures described above are of great value in producing temporary arrest of hæmorrhage and in preventing the development of gross sepsis, it must be clearly realized that the lesions are merely local manifestations of general disease and therefore adequate treatment must embrace control of the causal condition as described in the appropriate sections.

*General Measures.*—The multiplicity of remedies recommended for the treatment of purpura is itself an indication that none of them can be held to have consistently a specific action in the control of hæmorrhage.

*Adrenaline and Calcium.*—Where capillary permeability rather than thrombocytopenia appears to be the particular defect, or where allergy is suggested by clinical examination, *i.e.*, the coexistence with purpura of urticaria, cedema, or arthritis, adrenaline subcutaneously in 5 to 10 minim (0.3 to 0.6 c.c.) doses three times a day and calcium lactate, 30 gr. (1.8 gm.), four times a day by mouth and/or calcium gluconate, 10 c.c. intramuscularly once a day, are indicated.

*Vitamins.*—Where a history of dietary deficiency is obtained, with particular reference to fresh fruits and vegetables, and in patients suffering from chronic diseases and infective states both chronic and acute, the administration of vitamin C is worthy of trial, since this vitamin plays a rôle in the maintenance of the integrity of capillary endothelium. The quickest way to repair the vitamin C deficiency is by the parenteral administration (subcutaneously, intramuscularly or intravenously) of ascorbic acid. Suitable preparations for this purpose are issued in ampoules containing 500 mg. of vitamin C, 1 to 2 ampoules being given daily for a week. At the same time, oral treatment should be commenced by ordering 1 to 2 tablets of 50 mg., two to three times daily, or the juice of six oranges daily. A failure to obtain results within a week would suggest that the capillary permeability is not conditioned by vitamin C deficiency.

Recent research by Szent-Györgyi and others indicates that the factor concerned with capillary permeability is not vitamin C but another substance called vitamin P, which is found with ascorbic acid in paprika, hips and lemon juice. Vitamin P has not been isolated in a pure state, but citrin, prepared from oranges and lemons, and hesperidin, a crystalline compound of the flavonone group, have been found under experimental conditions, both in human beings and animals, to have some effect in increasing capillary resistance. Hesperidin is available under the trade-name of "Permidin" (Glaxo) in tablets each containing 150 mg. The recommended dose is two tablets *t.i.d.* Recent work suggests that the active agent in citrin is a derivative of flavone to which the name Rutin has been given. It is obtained from the leaves and flowers of buck-wheat. It is given by mouth in tablets containing 20 mg. and the dosage is stated to be from 20 mg. to 40 mg. thrice daily. Remarkable results have been claimed for the drug in hereditary hæmorrhagic telangiectasis in which the bleeding tendency is said to be controlled within 24 hours of the start of treatment. Other workers have stated that the increased capillary fragility which occurs in a proportion of cases of hypertension may be restored to normal. Treatment must be continued for two or three months to achieve this result. If independent confirmation is forthcoming, this work is of great clinical importance, since

it has been shown that the incidence of vascular accidents including apoplexy is very much higher in hypertensive patients with abnormal capillaries than in those with normal capillary fragility. Further time must elapse before the therapeutic value of Rutin in the control of hæmorrhagic conditions can be properly assessed.

For details regarding the use of vitamin K, see p. 512.

*Commercial Liver Extracts.*—These have been recommended by various workers in doses of 2 to 4 c.c. intramuscularly once daily. In our experience they are of little value except when a megaloblastic anæmia is present as well.

*Commercial Hæmostatic Preparations.*—There are many preparations on the market which are claimed by the manufacturers to have beneficial effects in the control of bleeding. Such claims are invariably backed by testimonials from practitioners who fail to realize that the value of hæmostatic preparations is difficult to assess because spontaneous cessation of hæmorrhage frequently occurs in the secondary forms of purpura. Of such preparations the best known are hæmoplastin, hæmagulen and thrombin coagulant.

In general our experience suggests that the results obtained from commercial hæmostatic preparations are unsatisfactory with the exception of tissue extracts for local application.

*Snake Venom, Foreign Protein, X-rays to the Spleen.*—Desensitization with gradually increasing doses of foreign protein such as horse serum or of moccasin snake venom given parenterally at intervals of a few days was claimed by certain writers to produce symptomatic improvement in a considerable proportion of cases of purpura. The fact that these measures are seldom used to-day suggests that the original claims were, to say the least, over-optimistic. Repeated applications of X-rays to the splenic area in cases of idiopathic thrombocytopenic purpura failed in our experience to improve the bleeding tendency or to produce an increase of thrombocytes.

From what has been said it must be apparent that none of the methods of treatment discussed above can be held to have been proved wholly satisfactory. It is probable that the beneficial effects obtained in many cases can be explained on the basis of a spontaneous remission of the hæmorrhagic state rather than as a direct result of the treatment. Nevertheless, where life is not in danger, one or a combination of the methods described can be tried together with the local and general measures outlined above. We would, however, earnestly offer this advice, namely, that should the hæmorrhagic state not be controlled within a few days and a progressive deterioration of the patient's health occur, the measures indicated under Group III should be instituted at once. Otherwise the tendency to bleed may coincidentally increase with the advancement of anæmia, and the ability to withstand the dangers associated with the measures in Group III progressively decrease.

### III. PURPURA WITH SEVERE HÆMORRHAGE

In this group are placed the patients whose lives are endangered by severe hæmorrhage, especially from the mucous membranes, which cannot

be controlled by the simple measures described above. Such cases are divisible into two types:—

- (a) In which the intractable purpura is associated with the terminal stages of certain diseases from which there is no hope of recovery, *e.g.*, aplastic anæmia, leukæmia, chronic nephritis with uræmia, etc. If such a diagnosis is established the patient should be allowed to die.
- (b) Where the severe bleeding is part of the disease idiopathic thrombocytopenic purpura. If vigorous treatment is immediately instituted on the lines described below, life can be saved and health restored in the great majority of cases. Only two methods need be considered, *viz.*, blood transfusion and splenectomy.

**Blood Transfusion.**—In many cases a single transfusion of 1 pint of fresh blood (see p. 933 *et seq.*) may be sufficient to control the hæmorrhage. In others it may be necessary to repeat the transfusion at intervals of from three to four days on several occasions. For the subsequent transfusions the amount of blood advised is 250 c.c.

**Splenectomy** is indicated as an emergency measure in patients who are exsanguinated and in whom the bleeding is not controlled by blood transfusion. The operation should be preceded and if necessary followed by transfusion of blood. The risks of emergency splenectomy are high, the mortality varying from 10 to 30 per cent. in different hands, but the risks from the hæmorrhagic state in these intractable cases of severe purpura hæmorrhagica are even greater. The principal reason why patients are allowed to reach this dangerous stage of shock is the continuation for too long periods of the measures outlined in Group II. We wish to point out again that splenectomy should never be performed as an emergency operation without first trying the effects of intravenous blood transfusion. It should also be remembered that many cases of idiopathic thrombocytopenic purpura in children recover spontaneously if life can be prolonged beyond the period of acute hæmorrhage, whereas, in adults, the disease is usually chronic although the onset may be acute. Accordingly in children blood transfusions should be given repeatedly until it becomes quite clear that spontaneous recovery is less likely to occur than death from continued hæmorrhage. Then, and only then, emergency splenectomy should be done as a last resort. In adults the chances of spontaneous recovery are less, and therefore splenectomy should not be postponed for so long, although blood transfusions should certainly be given a fair trial.

The second group of cases in whom splenectomy should be advised consists of patients with chronic thrombocytopenic purpura whose health and efficiency are being continuously impaired from recurrent hæmorrhage, which is only partly controlled by any of the measures mentioned above. As no emergency exists, the patient can be prepared for operation by the general measures outlined above together with iron and blood transfusions, repeated if necessary to bring the hæmoglobin to a safe level (70 to 80 per cent.) and control the tendency to bleed. The operative mortality in this group in skilled hands is less than 5 per cent.

Immediately following, or within a few hours of removal of the spleen, capillary oozing in all situations ceases, and with the help of iron the blood

level will be restored to normal within two months. Symptomatic cure occurs in at least 80 per cent. of cases, although in some individuals qualitative changes in the blood picture (thrombocytopenia) may still remain.

### HÆMOPHILIA

Hæmophilia is a hereditary disease characterized by a delay in the coagulation time of the blood and a tendency to recurrent hæmorrhages. Males only are affected, while transmission of the disease is solely through females of hæmophilic stock.

The relative rarity of the disease and the spontaneous fluctuations in the tendency to bleed which occur make the merits of any therapeutic measures difficult to assess. Treatment may be considered under three headings:—

**Preventive Treatment.**—(a) Since the disease is a hereditary one, an effort should be made to control its spread by eugenic measures. Females born of hæmophilic stock should be told that for the sake of posterity child-bearing must not be undertaken; (b) Prophylaxis of attacks of bleeding is obtained by regulating the patient's mode of life and activities so that the chances of trauma are reduced to a minimum. The dangers of trivial injury should be explained to the patient or his parents; (c) Proper preparations for any operative procedure should be undertaken.

**Treatment during an Attack of Bleeding.**—*General Treatment.*—Energetic measures should be immediately instituted to stop the hæmorrhage, since, if anæmia is allowed to develop, the resulting dilution of the blood which occurs lowers the concentration of the blood-clotting elements. Hence the use of commercial hæmostatic sera and of drugs, such as calcium, adrenaline, ergot, parathyroid extract, œstrogenic substances, etc., cannot be recommended, because there is little evidence that they are of value in altering the course of the disease, and their employment may even be a danger, since their use involves delay in the adoption of measures of proved value. If the site of hæmorrhage is not accessible, or if the bleeding is severe, transfusion of 1 pint of citrated blood should be undertaken. Recent work has shown that fresh blood is preferable to blood which has been stored in a bank. This usually controls the hæmorrhagic tendency for several days and the transfusion can then be repeated if necessary. In less severe cases the intramuscular injection of 10 to 30 c.c. of whole blood may suffice. In children the intraperitoneal transfusion of blood has been shown to be a satisfactory pre-operative measure. An impressive step forward has been made by Cohn and his co-workers (1944), who have produced by fractionation of plasma a globulin fraction which, when injected intravenously in a dose of 200 to 600 mg., produces immediate reduction of the coagulation time in hæmophilia to normal and frequently maintains it there for many hours. It is expected that even more potent fractions of plasma will be obtained by this method. British physicians are eagerly awaiting a supply of this material.

*Local Treatment.*—If bleeding takes place from an accessible situation, e.g., nose, tooth socket or a cut, the bleeding area should be gently cleaned and useless clots removed. A dressing soaked in a solution of rabbit globulin, if available, or of Russell's viper venom (see p. 505) or normal fresh whole blood or serum should then be applied and kept firmly in position. Special

bandages, packs, plates or splints may be required to maintain an effective pressure and reduce movement to a minimum (for details, see p. 506). Hæmatomas and swollen joints should not be opened or aspirated, and orthopædic treatment should be undertaken by the use of splints, cages, etc., to put the parts at rest until pain and swelling disappear. After the acute symptoms have subsided, heat, gentle massage and passive movements are indicated. Open wounds should be left open. Closure by sutures may result in the formation of large hæmatomata.

**Treatment between Attacks of Bleeding.**—*Induction of Protein Hypersensitivity.*—The suggestion of Vines, that stimulation of the thrombogenic functions of the somatic cells may be produced by the induction of a modified form of anaphylactic shock, has received the enthusiastic support of Mills, who claims that so long as a state of hypersensitivity is maintained the coagulation time of the blood is kept low. The method recommended by Mills may be summarized as follows: Sheep or hen serum is used. An intradermal injection is first given to ascertain whether or not the patient is already sensitive. If not, 3 or 4 c.c. are injected intramuscularly and fourteen days later another intradermal injection is given. An urticarial wheal should now appear, indicating that the patient is sensitized. If the coagulation time has not now shortened sufficiently, one should give further intradermal injections at weekly intervals, in different skin areas. This does not tend to reduce the general sensitivity. Thereafter, the coagulation time should be the guide as to the frequency of the intradermal injections. Sensitivity usually lasts for about a year, and at the end of that time it should be renewed by another intramuscular injection of the same or a different protein. Particular care should be taken to avoid injection of the serum subcutaneously while an intradermal injection is being given, as in this way a generalized reaction may be produced which may precipitate the patient into a hæmorrhagic state.

Eley and Clifford treated eight hæmophilic children by the above method, using intradermal injections of horse serum at fortnightly intervals. They confirm Mills' finding that a rapid and marked reduction in the coagulation time of the capillary blood could be obtained and maintained, but the coagulation time of the venous blood was unaltered. The therapy was of convincing benefit in the prevention or control of bleeding from superficial injuries, but was of little value when large vessels were injured, or for the prevention of effusions into joints or of hæmatomas.

**Placental Extract.**—Eley and his co-workers in Boston have made a study of the value of the oral and intramuscular administration of extracts made from human placental tissues. Fifteen hæmophilic children were treated, and the data presented clearly show that a marked reduction of both the capillary and venous coagulation times was obtained. The clinical effects appear to be superior to those produced by protein hypersensitivity.

**Egg White.**—Timperley, Naish and Clark treated thirteen unselected cases of hæmophilia by intravenous or intramuscular injections of a substance which they have prepared from egg white incubated at 37° C. in the presence of potassium bromide. They claim that the clotting time of the blood was reduced and hæmorrhage was controlled. Timperley has since claimed to have confirmed these findings in a further series of cases. It should be noted, however, that these claims have not been confirmed by several independent hæmatologists.



In conclusion, it would appear that in selected cases some benefit may result from the forms of treatment detailed above. An extended trial under controlled conditions is obviously desirable, and an open mind must be kept until this is done in view of the remarkable variations which spontaneously occur in the hæmophilic state.

*General Measures, including Diet.*—The general health should be maintained at as high a level as possible by the administration of a well-balanced diet and by regulated exercise in the fresh air and sunshine. Since there is some evidence to support the view that the coagulability of the blood can be influenced favourably by the absorption of protein from the intestine, a high protein diet has been recommended as a prophylactic measure. In addition to a moderate intake of protein at each of the three main meals, Mills recommends giving a glass of milk or an egg nog between meals and once during the night. If anæmia is present, iron should be prescribed in adequate doses (see p. 470) and treatment continued until a normal hæmoglobin figure is obtained.

*Removal of Septic Foci.*—It is well recognized that sepsis can play an important part in lowering the general health, in retarding the response of the hæmopoietic tissues to hæmorrhage, in damaging the endothelial lining of blood vessels and in initiating arthritis or influencing it unfavourably when it has occurred. Accordingly, despite the risks involved, obvious septic foci must be eradicated. The operation should be postponed, if possible, until the disease is in a quiescent state. Transfusion of blood before and after the operation, as well as other measures mentioned above, may be necessary for the control of hæmorrhage.

### HYPOPROTHROMBINÆMIA

It has now been clearly shown that the bleeding tendency commonly seen in cases of obstructive jaundice and chronic biliary fistulæ is due to deficiency of a fat-soluble substance called vitamin K, which is not absorbed owing to the failure of adequate fat digestion consequent on the absence of bile from the small intestine. Defective absorption of vitamin K may also occur in severe diarrhoeal diseases such as sprue and ulcerative colitis, and in hepatic disease. Lastly the bleeding tendency of newborn infants has been shown to be due to vitamin K deficiency. In all such cases the prothrombin level in the blood is very low, and this is apparently due to the fact that vitamin K is an essential constituent of prothrombin or is necessary for its manufacture by the liver. The oral administration of an extract of alfalfa (rich in vitamin K), e.g., "cerophyl" emulsified in human bile or in a solution of sodium taurocholate, to patients with obstructive jaundice rapidly raises the prothrombin level and brings about cessation of the bleeding tendency. An improvement in this form of therapy was achieved by the manufacture of more concentrated extracts dispensed in oily solution in capsules for oral administration.

All forms of vitamin K therapy by mouth have the disadvantage that bile salts must be given at the same time in cases of obstructive jaundice; otherwise there will be little or no absorption of the vitamin. This difficulty has now been overcome by the discovery that menaphthone (B.P.) (2-methyl-1, 4-naphthoquinone) possesses vitamin K activity and is very

effective when injected intramuscularly dissolved in oil. Solutions of this substance suitable for intramuscular injection are now available commercially, containing 5 mg. in each ampoule (1 c.c.), and a single injection of this amount has been shown to produce a rapid rise in the prothrombin level in suitable cases. When surgical intervention is planned in cases of obstructive jaundice with hypoprothrombinæmia, 1 c.c. should be injected daily for three days before and after operation. Similarly the parenteral administration to the mother immediately before parturition or to the infant will prevent or arrest neo-natal bleeding due to hypoprothrombinæmia. The injections may cause some pain, but this slight disadvantage is more than counterbalanced by the efficacy of the treatment and the ease of its administration as compared with oral therapy by solutions of vitamin K and bile salts. Blood transfusion used to be the only form of treatment which could be relied upon to check the hæmorrhage which so often complicates operation in jaundiced patients. Now it is rarely necessary if the specific therapy described above has been carried out, except when severe hepatic damage is present. Under such circumstances the liver may be unable to manufacture prothrombin, and the pre-formed product, as supplied by whole blood given by transfusion, may be required. Practitioners should realize that vitamin K is of no value in any hæmorrhagic disease other than hypoprothrombinæmia.

#### FIBRINOGENIA

Fibrinopenia is an exceedingly rare disease. According to some authorities the deficiency of fibrinogen is a hereditary defect. The disease simulates hæmophilia in that a prolonged coagulation time is found. The diagnosis depends on the establishment by chemical analysis of the absence of fibrinogen in the blood. The hæmorrhagic manifestations are stated to be rarely so grave as in hæmophilia, but when present the only therapeutic measure of any value is transfusion of whole fresh blood which temporarily supplies the missing factor, fibrinogen.

### AGRANULOCYTOSIS

*(Agranulocytic Angina; Granulocytopenia; Malignant or Primary Neutropenia)*

Agranulocytic angina is a rare disease characterized by acute onset, pyrexia, necrotic lesions mainly in the buccal cavity and marked leucopenia with extreme lowering or complete absence of neutrophil polymorph cells. Rarely the course of the disease is chronic with periodic exacerbations. The condition is due to arrest of granular white cell formation in the bone-marrow.

The term "agranulocytic angina" does not include the severe leucopenias which may occur in septicæmia, acute infectious fevers and aplastic anæmia, or as a terminal event in long-continued debilitating diseases.

**Prophylactic Treatment.**—Recent work has shown that cases of agranulocytic angina may be divided into two groups: (1) in which the cause is

unknown, and (2) secondary to the administration of certain drugs, especially amidopyrine, phenacetin, the arsphenamides, certain gold salts, thiouracil, and the sulphonamides. These drugs possess in common the benzene ring with an attached  $\text{NH}_2$ , or amino group. The most important, because of their very widespread use, are amidopyrine and the sulphonamides, and it has been estimated that these preparations are the cause of the great majority of cases of agranulocytic angina.

The drugs mentioned above are used with great frequency, but agranulocytic angina rarely develops. This suggests that the disease occurs only in those individuals in whom there is an idiosyncrasy or hypersensitivity to the particular drug employed. This conclusion is supported by the fact that the development of agranulocytic angina bears no relation to the amount of the drug taken, and in patients who have recovered from the disease a minute dose may cause an immediate and profound fall in the number of circulating granulocytes. Unfortunately there is no method whereby the development of such sensitivity may be predicted, and the value of amidopyrine, the organic arsenicals, gold salts, thiouracil and the sulphonamides is so great that the serious results which occur in a very small proportion of individuals treated with these drugs cannot be considered as a contraindication to their use in suitable cases. Nevertheless, the possibility of an untoward reaction should be borne in mind and the earliest symptoms of intolerance, namely, drowsiness, weakness, exhaustion and unexplained pyrexia, should immediately raise the suspicion of agranulocytosis, and, if leucopenia is found, the administration of the drug should be stopped at once. In elderly persons and in those debilitated by long-continued illness, it is a wise precaution to perform leucocyte counts every week during treatment by any of the drugs mentioned, and the development of a significant degree of leucopenia should be a signal for the immediate withdrawal of the drug. The ease with which lay persons may purchase proprietary preparations which contain amidopyrine and are sold under trade-names giving no information regarding their composition is to be deprecated. Amidopyrine and phenacetin should be available to the public only through the medium of non-renewable prescriptions given by physicians. It is important to realize that although prolonged ingestion of these leucotoxic drugs only rarely produces agranulocytic angina, it causes not infrequently a moderate leucopenia which may markedly reduce resistance to infection.

**Curative Treatment.—General Measures.**—The general nursing and care of a patient with agranulocytic angina are the same as for any acute febrile illness. The application of an ice-bag to the neck may relieve the pain in the throat, and the diet in the acute phase should be of high caloric value, and fluid or semi-solid because of the dysphagia which is frequently a troublesome symptom.

**Local Treatment.**—Until recently the treatment recommended for the lesions of the mouth and throat consisted of repeated application of 50 per cent. hydrogen peroxide followed by a solution of 40 gr. (2.4 gm.) of citric acid in 1 oz. (28.4 c.c.) of water, diluted 1 part in 7 before use. It is now believed that the local application of penicillin by spray, by insufflation, or by pastilles (see p. 93) is far more effective.

**Treatment of the Agranulocytosis.**—In every case of agranulocytic angina exhaustive inquiries should be made regarding drugs taken by the patient,

and any preparations with leucotoxic properties should, of course, be at once withdrawn. In a proportion of cases recovery then occurs rapidly without further specific treatment. Since the cause of death in agranulocytosis is directly attributable to bacterial invasion of the tissues and blood stream, the single most important therapeutic measure is the prevention and cure of infection. Until recently the sulphonamide drugs were used for this purpose, although they had the serious disadvantage of having leucotoxic properties. The position, however, has now been entirely altered by the introduction of penicillin, which fortunately has no depressing effects on the production of immunity or on hæmatopoiesis. Every case of agranulocytosis, whether idiopathic or symptomatic, should receive immediately local and general penicillin treatment on the lines described on pages 89-91. The writers can testify from personal experience to the remarkable results which may be expected. Where the cause of the agranulocytosis is known and has been removed, no treatment may be required other than the administration of penicillin. In other cases where the cause is unknown, or where, despite penicillin therapy, the agranulocytosis persists, attempts must be made to stimulate the production of granulocytes. Leucocyte extracts, parenteral liver therapy and the application of X-rays have been used for this purpose and all have proved disappointing. Repeated daily transfusions of 250-500 c.c. of fresh blood have been advocated. While this procedure seldom results in a sustained rise in the leucocyte count, its adoption is justified because of the temporary symptomatic improvement and reduction in pyrexia which may result. The parenteral administration of the sodium salts of pentose nucleotide has been widely recommended for this purpose. The product is marketed under the names of Pent-nucleotide, Pentide and S.P.N., and is supplied in the form of a solution, in 10 c.c. vials, each containing 0.7 gm. of the salts. Although many favourable results have been published regarding the efficiency of this form of treatment, recent investigations suggest that the original claims were over-optimistic. Nevertheless, pentnucleotide should be given in all severe cases of agranulocytosis which are not responding clinically and hæmatologically to penicillin. 10-20 c.c. of pentnucleotide should be injected deeply into the gluteal muscles twice daily for the first three days, followed by 10 c.c. once or twice daily for a week. Total white cell and differential counts should be made each day. In favourable cases an increase in the granular leucocytes occurs, usually between the third and fifth days, less often on the first or second day, with accompanying clinical improvement. The intramuscular injection of 10-20 c.c. of pentnucleotide may be accompanied by considerable discomfort or pain. This may be reduced by vigorous massage and the site of the injection should be varied. Serious general reactions occur so frequently when the drug is given intravenously that it is usually advisable to avoid this route of administration.

Recently, good results have been claimed from the administration of pyridoxine, a member of the vitamin B<sub>2</sub> complex (150-200 mg. daily by mouth or intravenous injection), especially in cases of agranulocytosis due to thiouracil. These claims have been rejected by other workers. In our experience folic acid is ineffective for this purpose.

*Prevention of Relapses.*—All patients with agranulocytic angina due to drugs should be warned against taking the offending preparation in any form in the future.

## DISEASES OF THE RETICULO-ENDOTHELIAL SYSTEM

### RETICULOSES, INCLUDING HODGKIN'S DISEASE, RETICULUM CELL SARCOMA AND LYMPHOSARCOMA

Some authorities include under this heading not only the conditions listed above and the diseases of lipoid metabolism but also all varieties of leukæmia, on the basis that all types of blood cells are developed from the reticulo-endothelial system.

From the clinical point of view it is simpler to limit the term reticuloses to changes involving the fixed reticulum or endothelial cells, giving rise to tumour-like formations in many situations, particularly the lymph nodes. The reticuloses are characterized by progressive enlargement of the lymphoid tissues, commencing in any situation and generally becoming widespread.

**Treatment.**—Like the leukæmias, the reticuloses are invariably fatal, but the duration of life varies within the very wide limits of a few weeks to about ten years. The general condition of the patient may, for a time, be considerably improved and the progression of the glandular enlargement may be much delayed by irradiation therapy (see p. 521).

Arsenic is of value in improving the patient's general health, and should be given in the dosage described on p. 519, and iron (see p. 470) should be prescribed in an attempt to correct the hypochromic anæmia which usually accompanies the condition. Lotio phenolis (B.P.C.) and lotio picis carbonis alkalina (B.P.C.) are useful preparations for allaying the pruritus which is occasionally a troublesome symptom.

The general measures which should be adopted are the same as for the leukæmias (see below).

Gordon prepared from emulsions of glands a suspension of a virus which he claims to be the infective agent causing Hodgkin's disease. A few cases have been treated with injections of a vaccine made from the virus with apparently beneficial effects, but not in sufficient numbers to enable one to form conclusions regarding the value of this form of therapy.

### DISEASES OF LIPOID METABOLISM

Gaucher's disease.

Niemann-Pick disease.

Hand-Schüller-Christian disease.

There is no specific treatment for this group of rare diseases. The presence of hypochromic anæmia is an indication for the administration of iron (see p. 470). Some authorities recommend splenectomy in all cases in which the diagnosis of Gaucher's disease has been established, because of the great discomfort caused by the huge splenic tumour in the late stages of this disease. In our opinion the operation is not justified because hepatic enlargement occurs more rapidly after splenectomy. In the Hand-Schüller-Christian syndrome hypercholesterolaemia may or may not be present. It is claimed that when a high blood cholesterol level is found it may be reduced by a diet low in fat, and that this may retard the progress of the disease. X-ray therapy is of no value in Gaucher's disease or in Niemann-Pick disease, but will cause a disappearance of the tumours and of the

osteolytic areas in the bones in the Hand-Schüller-Christian syndrome. Although the general health may be little improved, the liability to spontaneous fractures is reduced and pressure symptoms are ameliorated. In this disease there is obvious pituitary dysfunction resulting in diabetes insipidus and retarded growth, etc. (see pp. 442, 444).

## THE LEUKÆMIAS

The leukæmias are characterized by qualitative or quantitative changes in the circulating white cells due to an abnormal proliferation of the leucopoietic tissues, the cause of which is unknown. The proliferation affects the lymphoid, myeloid or more rarely the monocyte-forming tissues. In the acute leukæmias the total white cell count may be little altered and the diagnosis is made by a differential count which shows the presence of an extremely high proportion of stem cells which may be lymphoblasts, myeloblasts or monoblasts. In the chronic leukæmias, on the other hand, the total white-cell count is usually greatly increased, while the stem cells are absent or scanty, and immature cells form only a proportion of the total white cell count.

The need for accurate diagnosis is apparent when it is realized that the acute forms of leukæmia always terminate fatally within a period of weeks or at the most months, and are materially uninfluenced by any form of treatment, while the chronic forms, although inevitably fatal, can be modified favourably by modern methods of treatment, particularly in regard to improving the well-being of the patient and prolonging economic efficiency.

## CHRONIC LEUKÆMIAS

The treatment of chronic myeloid, lymphoid and monocytic leukæmias is considered together, since the same measures with minor modifications are suitable for all three forms.

**General Measures.**—The average expectation of life in the chronic leukæmias has been found to be about three years. No matter what form of treatment is employed a fatal termination invariably occurs. Nevertheless, modern treatment with X-rays has considerably increased the period of economic efficiency and prolongs life for a few months. Accordingly, the patient should be advised to continue at his occupation or routine duties for as long as possible. Common-sense measures should be adopted regarding the regulation of the patient's life in regard to overwork, excessive exertion and chilling. Infections produce a marked deterioration in the health of patients with leukæmia. Hence, such patients should avoid close contact with persons suffering from colds in the head, sore throats, influenza, etc., and places where persons are crowded together during epidemics. Should a patient with leukæmia contract a mild infection, he should treat it much more carefully than a normal individual and remain in bed until the condition has completely cleared up.

Careful instructions should be given to the patient that, while exercise in the fresh air, such as walking, golfing and bicycling, is of value in maintaining health, the amount undertaken should always be well within the limit of his tolerance. An ordinary mixed diet should be advised which should contain ample quantities of the foods valuable for blood regeneration

(see p. 468), and the total calories should be high in view of the increased basal metabolic rate so frequently present in leukæmia. This can easily be attained by prescribing additional quantities of butter, cream, bacon and the foods rich in carbohydrate.

Eventually, despite all treatment, emaciation and anæmia develop and the patient will have to give up his occupation and spend more and more time in bed. It is at this stage that blood transfusion is of value in improving the patient's general health and thus allowing the continuation of irradiation therapy.

In the terminal stages, when anæmia is severe and hæmorrhage and sepsis are occurring locally in the nose, mouth, etc., the measures outlined on pp. 505-506 should be taken.

**Irradiation Treatment.**—Irradiation is the most satisfactory method of treatment available for chronic leukæmia and should be adopted in every case. The patient should be in hospital for the first course of irradiation, but if for some reason this is impracticable, he may be treated as an out-patient under close supervision. On p. 521 will be found a discussion on deep X-ray therapy.

Anæmia itself is not a contraindication to the use of X-rays. On the contrary, since the anæmia is due to a crowding out of erythroblastic tissues by leucoblastic tissue, properly controlled irradiation is generally followed by a rise in hæmoglobin and circulating erythrocytes. Transfusion of blood may be employed in anæmic individuals undergoing irradiation therapy in order to tide them over the period which must elapse before regeneration of red cell marrow can occur.

A time will come when destruction of erythroblastic tissue occurs, with the production of anæmia which cannot be controlled by iron or blood transfusion. When this stage has been reached active treatment should be stopped, and morphia or other symptomatic measures used to keep the patient comfortable.

**Radio-active Phosphorus.**—Radio-active phosphorus is prepared by bombarding phosphorus by the cyclotron. It is given therapeutically by the intravenous route as a solution of radio-active dibasic sodium phosphate. Its radio-active properties have a steady rate of decay, and this is claimed to be one of its chief advantages, since if given in proper dosage it is held to have no long-range harmful effects on the body. Radio-active phosphorus has been used in America for the treatment of leukæmia and polycythæmia vera. The quantity of radio-active material and frequency of injections are adjusted according to the individual's response to treatment. The danger of causing aplastic anæmia from overdosage must never be forgotten. The results reported in leukæmia appeared to be similar but little, if any, better than those expected from deep X-ray therapy. At the time of writing, radio-active phosphorus is not available in Great Britain for therapeutic purposes.

**Drug Treatment.**—Of the numerous drugs recommended for the treatment of leukæmia, only urethane, arsenic, benzol, iodine, iron and liver extract need be mentioned.

*Urethane* (ethylcarbamate) was found to have a growth-inhibiting effect on animal tumours and this suggested its trial in the leukæmias. In 1946 Paterson, Haddow, Thomas and Wilkinson reported on the effects produced in 19 cases of myeloid and 13 cases of lymphatic leukæmia. Remarkable

palliative results were recorded, in many cases comparable to those obtained by irradiation both in degree and in their certainty of relapse. The drug was dispensed as a mixture containing 1 gm. to a tablespoonful of chloroform water sweetened with syrup auranti. The dosage used varied considerably but was usually around 3 to 5 gm. daily. The time taken to reduce the white cell count to approximately 20,000 varied from 11 to 36 days. Reduction in the size of the spleen and lymph nodes resulted, with improvement in the patient's general health. Nausea was a common toxic effect, and when accompanied by vomiting necessitated a discontinuation of oral treatment. Rectal administration was sometimes successfully employed in such cases. Treatment was most effective in chronic myeloid leukæmia, less effective in lymphatic leukæmia, and least effective in all forms of acute leukæmia. This has also been our experience. On the whole we have not been favourably impressed with the results achieved. Sufficient time, however, has not elapsed to decide finally whether urethane is superior to X-rays in prolonging life and in maintaining the patient in a better state of health. All that can be said at present is that a new drug has been introduced which has effects comparable to X-rays and that it is probably more effective and less toxic than arsenic.

*Arsenic*, like irradiation, is only palliative. Before the advent of irradiation it was the most potent therapeutic agent available. It is mainly in chronic myeloid leukæmia that beneficial effects have been claimed for it. Recently, as a result of the publications of Forkner and Scott, its use has again been recommended. We feel, however, that it is inferior in its action to irradiation and has, in addition, definite disadvantages, particularly the unpleasant symptoms of chronic arsenical poisoning, which no longer entitle it to a prominent place in the treatment of the leukæmias. Hence we do not agree with certain workers that irradiation treatment should not be employed until arsenic has been given a full trial. It is usually stated that arsenic should not be given during treatment by X-rays because of the dangers of secondary radiation, but this risk is so slight that it need not be considered. Arsenic will certainly not succeed in cases which have reached the stage of insensitivity to irradiation. Accordingly, we can recommend arsenic only to those patients with leukæmia for whom irradiation therapy is difficult or impossible to procure.

Arsenic is generally given in the form of Fowler's solution (liquor arsenicalis). The initial dose should be 3 minims (0.17 c.c.) three times a day, and the dose increased by 1 minim (0.06 c.c.) per dose every two days. This is continued until definite toxic symptoms (nausea, vomiting, diarrhœa, tinnitus, and a metallic taste in the mouth) are produced. This amount varies in different individuals from 30 to 60 minims (1.7 to 3.5 c.c.) daily. The earliest symptom of toxicity is anorexia, which may appear when the total daily dose is about 20 minims (1.2 c.c.), and it may be necessary to reduce the increments and prolong the intervals between them when this symptom occurs. It should be realized, however, that the patient must take the maximal quantity of arsenic which he can tolerate if results are to be produced.

When full toxic symptoms appear, indicating that the maximal dose has been reached, the drug should be discontinued for two or three days and then started again with about three-quarters of the previous dose. When the limit of tolerance has been reached or the optimal improvement



in the blood picture has appeared, the drug is gradually reduced in the manner in which it was increased.

*Benzol* is a powerful leucocytic poison. It is administered with olive oil in capsules, the initial dose being 0.5 gm. four times a day. The dangers of producing aplastic anæmia are in our opinion so great that they more than counterbalance the fall in the leucocyte count which coincidentally occurs. Accordingly, we recommend that benzol should not be used in the treatment of leukæmia.

*Iodine* has been recommended in the treatment of leukæmia, especially in the chronic lymphatic form in which a high basal metabolic rate has not infrequently been noted. While it is of some value for the relief of such symptoms as tachycardia, sweating and nervousness, it has little or no effect in the control of the blood picture. Accordingly, it should never be used alone, but only in combination with irradiation therapy. Lugol's iodine in doses of 5 to 10 minims (0.29 to 0.58 c.c.) three times a day is the preparation most commonly employed.

*Iron*.—An iron deficiency anæmia is common in chronic leukæmia and requires treatment with dieto-therapy and medicinal iron, as described on p. 470.

*Liver Extract*.—In the acute leukæmias and in the terminal stage of the chronic leukæmias a macrocytic anæmia develops with a high colour index and a red cell picture resembling pernicious anæmia. The macrocytosis is, however, the result of excessive activity in the remaining portions of erythroblastic marrow and is not due to a deficiency of the anti-anæmic factor. It is not surprising, therefore, that we have been unable to influence this terminal blood picture by liver or liver extract.

### ACUTE LEUKÆMIAS

Once the diagnosis of acute myeloblastic, lymphoblastic or monoblastic leukæmia is made, it should be realized that a fatal termination will occur within a few weeks. Splenectomy is contraindicated in this as in all forms of leukæmia, and X-rays and radium are generally held to aggravate rather than improve the condition. Urethane has only a limited temporary effect.

Blood transfusion and injections of penicillin are warranted only if for some specific reason it is desired to prolong life for two or three weeks, or to control infection or severe local hæmorrhage, particularly from the nose and mouth, which is interfering with the comfort of the patient. Accordingly, treatment is purely symptomatic, and sedatives such as morphia should be given in adequate amounts to make the patient comfortable.

### ALEUKÆMIC (SUBLEUKÆMIC) LEUKÆMIA

Aleukæmic leukæmia may be defined as a leukæmia in which the abnormal white cells are found to infiltrate the bone-marrow and many organs of the body although the white cell count is low or within normal limits. The differential count may be qualitatively normal or abnormal. Diagnosis obviously presents the greatest difficulty unless histological examination of the bone-marrow, obtained by biopsy, is undertaken. Aleukæmic leukæmia may occur in the acute form, clinically indistinguishable from the other acute leukæmias mentioned above, and in such cases treatment is purely symptomatic on the lines already described. In other cases the course is chronic and the question arises whether or not irradiation should be given. The

failure of the abnormal cells to enter the peripheral blood makes assessment of the degree of irradiation required extremely difficult. Accordingly, the risks of producing aplastic anæmia are serious, and for this reason some authorities hold that X-rays are contraindicated. Moreover, there is some evidence to suggest that occasionally irradiation therapy may precipitate an acute phase of the disease. We feel, however, that since the only hope of radically influencing the anæmia lies in the destruction of the leucoblastic tissue which is infiltrating the bone-marrow, irradiation therapy to the spleen or lymph glands should be advised if these organs are enlarged. Obviously, irradiation must be given tentatively in small graduated doses, using the erythrocyte and thrombocyte counts and the clinical state of the patient to assess its efficacy.

The other measures found to be of value in the chronic leukæmias should also be used in chronic aleukæmic leukæmia.

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H. W. FULLERTON.

## DEEP X-RAY TREATMENT OF POLYCYTHÆMIA VERA, LEUKÆMIA, AND RETICULOSIS

In the treatment of the above diseases X-ray therapy is the method of choice and the use of radium has been abandoned. Daily treatment in small doses is preferable to weekly or monthly treatments with large doses. In polycythæmia vera and in the generalized types of reticulosis it is now customary to irradiate the whole of the patient's body. In this so-called wide-field or "bath" treatment, the dosage employed is a mere fraction of what is required when localized treatment is given to each area of involvement in turn. Moreover, the patient is usually less upset by wide-field treatment and the benefit obtained appears to be more lasting. No skin reactions are produced and the head may be safely included in the field of treatment without danger of producing epilation. It is advisable, however, to protect the gonads so as to avoid the risk of sterilization. In chronic leukæmia irradiation of the spleen has in the past been the method most generally used. A satisfactory fall in the white cell count occurs and patients have been maintained in good health for several years. By confining the application to the region of the spleen, damage to the erythropoietic tissues in the bone-marrow is believed to be reduced to a minimum. Recently, cases of chronic leukæmia have been treated by the wide-field method, with hæmatological results equally as good as those obtained by the local irradiation of the spleen, together with the additional benefits mentioned above. In the writer's view, the wide-field method will be in the future the method of choice. Localized treatment may still be given in certain types of the reticuloses where the disease is confined to a limited group of glands.

When X-ray treatment is given the dosage must be carefully controlled by means of repeated clinical examinations and frequent blood counts, which, in addition to white-cell counts, should include periodic examination of the erythrocytes, hæmoglobin and platelets.

**Polycythæmia Vera.**—The immediate effects of treatment may not be obvious, since several weeks may elapse before the red cell count begins to fall. It is important therefore that treatment should terminate before there is any marked reduction in the red cell count. If treatment is carried on

too long there is a danger of producing aplastic anæmia. It is better to give too little than too much, because the course of treatment can always be repeated if too little has been given.

**Chronic Leukæmia.**—In leukæmia, treatment should be continued until the white cells fall to about 20,000 cells per c.mm. The rate of fall, however, is the most important guide to treatment. If the white cells fall rapidly, then treatment should be stopped before the above figure is reached. If they fall slowly, irradiation may be continued even after the count has reached 20,000. As mentioned above, it is most important that full blood counts should be made. In a case successfully treated the red cells and hæmoglobin rise as the white cell count falls and the patient's general health improves. When a fall in red cells and hæmoglobin coincides with a fall in the white cell count the patient is unlikely to benefit to the same extent. Under these circumstances blood transfusion may be of real value in helping to sustain the patient while awaiting the improvement in erythropoiesis.

**Generalized Reticulosis.**—In the treatment of the generalized reticuloses, the aim is again to improve the patient's general health. It is important that this objective should be kept in view, and it is better to have a fit patient with some enlarged glands than an ill patient with a complete regression of glandular enlargement.

In the localized reticuloses, in addition to regional irradiation, it is advisable to treat the adjacent lymphatic areas, even although they are not manifestly involved. This procedure seems to slow down the rate of advance of the condition. When the disease becomes widespread, "bath" treatments may be employed, though as a rule when localized reticulosis becomes widespread the disease has entered its terminal stages and little benefit is likely to be obtained by any form of treatment.

**Maintenance Treatment.**—Following the completion of the course of treatment of the above diseases full blood counts should be made at intervals of two to three months. Further treatment is indicated by deterioration of the patient's general health, and in the case of leukæmias and reticuloses it is more important to be guided by this rather than by the white cell count or by the degree of glandular enlargement. The hæmoglobin level and the red cell and platelet counts are of great value in immediate prognosis. Eventually a stage will be reached when further treatment results in no improvement in the patient's well-being or in the concomitant anæmia. In such cases, especially if purpura is present, treatment should be stopped irrespective of the blood count or of the size of the glands.

**X-ray Sickness.**—The symptoms of malaise and vomiting which sometimes occur during irradiation therapy are rarely produced by the small graduated doses of X-rays recommended above. If the condition develops, however, the course of irradiation should be interrupted and the patient should be confined to bed on a light diet and should be given small doses of a sedative, *e.g.*,  $\frac{1}{2}$  gr. (0.03 gm.) phenobarbitone t.i.d., until the symptoms have subsided. Injections of liver extract and the oral administration of glucose have been widely used, but it is doubtful whether they have any beneficial effect. Recently the parenteral injection of adrenal cortical extract (10 to 20 units) or desoxy-cortico-sterone-acetate ("Doca," 0.5 c.c.) has been suggested on the analogy that the features of X-ray sickness, *i.e.*, weakness nausea, vomiting and hypotension, are similar to those of adrenal insufficiency. Satisfactory results have been claimed.

R. McWHIRTER.

# DISEASES OF THE ALIMENTARY CANAL

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## DISEASES OF THE MOUTH

**A** CAREFUL examination of the mouth discloses the condition of the mucous membrane, teeth, gums, tonsils (see Pharynx, p. 705), tongue and salivary ducts. For convenience, the salivary glands may also be included here.

The discovery of an unhealthy state in any of these raises at once three important considerations on which treatment must be based:—

1. Some diseases of the mouth are of local importance only and strictly local treatment is required. Example—Parasitic stomatitis (Thrush).
2. Some are part of the clinical picture of a more general disease, to which the main therapy must be directed; but the mouth is not neglected in symptomatic treatment. Examples—Syphilis, acute specific fevers, scurvy, anæmias.
3. Some have wider implications as ætiological factors in general diseases. Efficient local treatment may be essential before the main disease can be dealt with adequately. Examples—Apical abscess and rheumatoid arthritis.

## THE MUCOUS MEMBRANE

Inflammation of the buccal mucosa (stomatitis) occurs in acute febrile diseases and in conditions of debility.

**Catarrhal (Simple) Stomatitis** is seen most frequently in the acute specific fevers, and its nursing care and simple treatment are dealt with on p. 4. Acute parotitis, referred to below, is an infrequent but well-recognized complication.

**Aphthous Stomatitis** (follicular stomatitis) may ensue in the debility after acute disease and in chronic gastric disorders of different kinds. Multiple small ulcers develop which heal rapidly under the treatment used for the catarrhal type. Rarely a stubborn ulcer may require a single application of the silver nitrate stick.

**Parasitic Stomatitis** (Thrush) is dealt with on p. 292.

**Ulcerative Stomatitis** (Vincent's Angina, **Ulceromembranous Stomatitis**) is a serious form of stomatitis with membrane formation and active ulceration often beginning on the tonsil but spreading to involve any part of the mouth or pharynx. The gums are generally swollen and ulcerated, and this is frequently the most striking lesion clinically. Diagnosis is made by examination of a stained film from the membrane or exudate, the characteristic fusiform bacilli and spirilla being found abundantly. Diphtheria must be excluded, and when the gums are involved, severe pyorrhœa and the spongy gums of scurvy (in both of which spirilla are generally present) may cause confusion. The chief complications are loosening and falling out of teeth,

inflammation of the cervical lymph glands and spread through the wall of the pharynx to produce acute mediastinitis. The last complication is rare, but hitherto almost always fatal.

This disease is contagious, and may assume almost epidemic proportions in conditions of privation and overcrowding. It has always been troublesome in the Fighting Services, and in the first world war was well known as Trench Mouth. In the second world war its occurrence was less frequent except among the crews of small ships.

Preventive treatment of the contagious disease is of first importance, particularly in the circumstances mentioned above as favouring its spread. Personal hygiene of the mouth, emphasized when necessary by suitable lectures or warnings, is essential; and the dangers of imperfectly washed spoons, forks, cups and other utensils must be pointed out. Both in the Services and in civilians its superficial resemblance to scurvy, when the gums are involved, has resulted in erroneous attempts at preventive treatment by administration of ascorbic acid, but no deficiency in vitamin C has been proved to exist when suitable controls were also examined. *Pyorrhœa alveolaris* (p. 525) is so commonly found in association with ulcerative stomatitis that adequate dental treatment, with removal of tartar, is an essential part not only of prophylactic but of curative treatment.

Until recently, whatever therapeutic measures were adopted, cure was seldom expected under ten days and relapses were common. Numerous local applications to the ulcerated mucosa were employed, including chromic acid as a caustic or as a ten per cent. solution, iodine, liquor arsenicalis and dyes such as gentian violet and flavine. Their multiplicity almost implies their inability to shorten the course of the disease, and they have all been superseded. Hydrogen peroxide (10 volumes) on a swab or diluted five times as a frequent mouth-wash, is still of value, chiefly acting mechanically by loosening membrane and bubbling away pus and debris from the ulcerated areas.

Penicillin now seems to be the best available treatment, administered locally in less severe cases by lozenges (each containing 500 units) which are allowed to dissolve slowly in the mouth. This treatment is often effective in three days, but should not be persevered with longer as the lozenges themselves may induce another form of stomatitis possibly due to the excipient. In severe cases, with ulceration of tonsils or pharynx, penicillin is best injected intramuscularly in high dosage three-hourly (p. 89), and is usually rapidly effective.

Prior to the use of penicillin, neoarsphenamine, 0.45 gm. intravenously, repeated if necessary, had been strongly recommended. If penicillin fails to cure within a few days, or if relapses are troublesome, intravenous arsenical treatment should certainly be tried.

### THE TEETH

The need for continued care of the teeth is still insufficiently appreciated in this country, and in Scotland at least the number of young adults entering our hospitals with complete dentures, or the necessity for them, can only be described as lamentable. With better attention to teeth, both personal and with the dentist's aid, many diseases of the alimentary system, and of other systems as well, could be avoided or minimized.

The main essential for a satisfactory first dentition in a child is to ensure a good diet for the mother during her pregnancy. The first teeth, and the period during which they are in use, are often neglected, but the permanent teeth are developing and maturing at that very time and serious defects may already have occurred in them before they actually erupt. The proper development of the teeth depends on adequate supplies of vitamins A, D and C, and of calcium, which are supplied by 1 pint of milk daily with orange juice and cod-liver oil. Enlarged tonsils and adenoids, by causing mouth-breathing, are still a common disturbing factor in early life, deforming the palatal arch. Special attention must be given to see that the permanent teeth, as they appear, are regularly spaced, not overcrowded and with a bite adequate for good mastication in future. If caries develops, whether in childhood or later life, the teeth must be filled, but root fillings and crowned teeth are to be avoided when possible, since both of these may lead to apical abscesses or granulomas which are often painless, but may be the cause of obscure illness.

A great deal of preventive work is now carried out by school dental officers, but it is the family doctor's duty to advise parents of all classes to train their children in the care of their teeth and to take them to a dentist at regular intervals.

In a number of diseases in adults, especially those affecting the alimentary system and joints, full advantage should now be taken of the modern technique of dental radiology; but even when dental or alveolar disease is found, much care and judgment are required by both doctor and dentist in deciding what line of treatment should be adopted. Wholesale extractions of teeth, even the whole of them at one sitting under general anæsthesia, are still frequently carried out; but this may be disastrous in the presence of extensive sepsis and fatalities are by no means unknown. In our view it is the doctor's function always to advise, in consultation with the dentist, on the necessity or otherwise for extractions, and on the prophylactic use of penicillin or sulphonamides (p. 78) before and after operation to neutralize bacteriæmia.

### THE GUMS

With sound teeth and good general health the gums seldom give rise to trouble, but in the absence of these, gingivitis, or inflammation of the gums, is very common.

**Acute Gingivitis** occurs in a variety of diseases, such as acute leukæmia, scurvy, and during treatment with some of the heavy metallic drugs (*e.g.*, bismuth and mercury).

**Chronic Gingivitis** may follow the acute type, but frequently appears insidiously in states of chronic ill-health or during convalescence from serious acute diseases. Marginal gingivitis is often named pyorrhœa, although more than the gums are finally involved.

**Pyorrhœa Alveolaris (Chronic Periodontitis)** is an inflammation of the gums, alveoli and, in later stages if unchecked, of the surrounding bone itself. The earlier the diagnosis is made the simpler and more conservative is successful treatment; but as pyorrhœa is unfortunately painless until late complications arise, the early stage is generally neglected by the patient and not seen by the doctor. The first sign is the appearance of a bright red

line along the gum margin, followed by atrophic changes in the interdental papillæ. Swelling, with gradual ulcerative erosion and finally disappearance of the projections of mucous membrane (interdental papillæ) between the teeth, is a cardinal sign of pyorrhœa and should always be looked for. Deep pockets thus arise from which pus can be squeezed; the pus contains micro-organisms of many varieties, and often includes the spirilla found in Vincent's angina. The inflammation spreads to the roots of the teeth, loosening them while destroying the alveoli. Finally, root abscesses and considerable rarefying osteitis may ensue. In the last stages the gums are no longer inflamed but shrunken, so that the teeth appear to be elongated and separated. This stage must never be forgotten in the investigation of rheumatoid arthritis for, although the teeth may appear sound, radiology may reveal root abscesses or extensive osteitis.

The treatment of pyorrhœa is always conservative in the early stages and only in late, severe or neglected cases is drastic dental surgery required. Close collaboration between doctor and dentist is essential, and the patient should always be warned that the treatment must be tedious and long-continued. The doctor's chief function in many cases is to deal with the causes of ill-health which have led to pyorrhœa, leaving the local condition to the dentist. The essential dental treatment may be summed up as efficient surgical drainage of the "pockets," removal of tartar which quickly deposits and measures to keep the mouth clean. Drainage of pockets is of first importance, and there should be no hesitation in using a fine scalpel to open up deep cavities or to excise parts of mucous membrane or interdental papillæ which hinder drainage. Local applications to the gums, mentioned in the section on Vincent's Angina (p. 523), are also useful for their astringent or cleansing action, but only when adequate drainage has been ensured.

**Stomatitis in Agranulocytosis** is dealt with on p. 514.

## THE TONGUE

Many diseases of the tongue are only of surgical importance, while others of particular interest to the physician are mainly part of the clinical picture of some more general disease (*e.g.*, the glossitis of anæmias and sprue) and do not necessarily require special local treatment.

## THE SALIVARY GLANDS

**Ptyalism**, or excessive secretion of saliva, has many causes; it occurs, for instance, in such diverse conditions as oral sepsis, trigeminal neuralgia, post-encephalitic parkinsonism and paralysis agitans, œsophageal irritation, mercury poisoning and gastric hyperacidity. In some cases no cause can be discovered, or the patient is simply noted to be of nervous type.

Treatment must be directed to the cause, but often symptomatic relief alone is possible. For the latter purpose belladonna should be used, the tincture being given in as small doses as possible to obtain the desired effect. In some cases  $\text{M}\text{v}$  (0.3 c.c.) t.d.s. suffices, in others much larger doses may be required. Sedatives in nervous patients or psychological treatment (ptyalism is common in aerophagy, p. 553) may be the correct line of action.

**Xerostomia**, or dry mouth, due to deficient salivation, is common in acute febrile diseases, and its treatment is included in the general care of the mouth and the correction of dehydration. Many cases are, however,

simply due to mouth-breathing or to sleeping with the mouth open, without actual diminution of secretion, and various forms of simple treatment may be successful—chewing gum, acidulated sweets, bitter tonics before meals and hard dry biscuits. Pilocarpine is the only drug likely to induce salivary secretion in cases resisting treatment; but in practice it should very seldom be required or employed.

**Parotitis** is most frequently seen as Mumps (p. 40), but occurs also as a complication of stomatitis. It was formerly common after surgical operations before the necessity for scrupulous care of the mouth and the giving of sufficient fluid during all serious illnesses, particularly those resulting in dehydration, was fully realized. Nowadays it is rare, but if encountered the treatment is at first conservative with simple hot moist applications to the region of the gland, frequently renewed, and plenty of fluid to drink. Abscess formation occasionally ensues and surgery is required.

## DISEASES OF THE ŒSOPHAGUS

### ŒSOPHAGITIS

Inflammation of the œsophagus may ensue after a foreign body or a corrosive poison has been swallowed. Many *foreign bodies* pass safely down the œsophagus and no treatment is required unless breathing is interfered with. A few become arrested, and should only be removed under direct vision through an œsophagoscope. This is an emergency operation of the greatest urgency; a few hours' delay may, and often does, result in the death of the patient. One of the commonest foreign bodies, especially in adults, is a stiff fish-bone, which may penetrate the wall of the gullet and lead to acute mediastinitis. The treatment is surgical, but the mortality is high. Unfortunately, the cause of the perforation is often quite unsuspected. *Corrosive poisons*, swallowed accidentally or with suicidal intent, generally burn the lips, mouth and pharynx, so that immediate diagnosis is easy. Apart from acute œdema of the glottis, which may rarely require tracheotomy, the brunt of the serious damage falls either on the narrow œsophagus or on the mucosa of the stomach. Acute sloughing or perforation of the œsophagus is likely to be rapidly fatal from severe shock. The patient is put to bed, the correct antidote given, if the poison is known, but otherwise nothing whatever is given by mouth. In corrosive poisoning, in contradistinction to other types of poisoning, no attempt to pass a stomach tube must be made. The main immediate treatment is to combat shock, and the agonizing pain demands an immediate injection of morphine.

**Simple Stricture.**—In patients who survive, stricture is common. The treatment of such cases is difficult, and should only be carried out by experts. The chief difficulty for the physician is to decide the time when gradual dilatation should commence—all acute inflammation must have subsided while dense cicatrization must be forestalled. In most successful cases the primary dilatation must be followed by subsequent courses of treatment, as gradual scarring and contraction may continue for a number of months.

### DYSPHAGIA

Difficulty in swallowing is generally the cardinal symptom of œsophageal disease, and when this occurs the first problem to decide is whether the diffi-



culty is due to an organic or functional cause. In one condition, referred to below, the difficulty is in starting the reflex act, but most commonly the fault is in the œsophagus itself. The gullet is, on the whole, firmly fixed in position at its two ends and in its course between them, and the patient can in consequence generally localize the seat of obstruction fairly accurately, pointing to the site with his finger. This is of real help in preliminary diagnosis, since certain conditions affecting the œsophagus are well known to have favourite sites.

*Dysphagia arising near the Junction of Œsophagus and Pharynx.*—Plummer-Vinson (Paterson-Kelly) syndrome. Diphtheritic palsy of the soft palate. Dysphagia in certain nervous diseases (e.g., bulbar paralysis). Hysteria.

*Dysphagia arising in the Mid-Œsophagus.*—Carcinoma. Organic stricture following corrosive poisons. Rarely, pressure of an aneurysm, mediastinal tumour, or retro-sternal goitre.

*Dysphagia arising near the Lower End of the Œsophagus.*—Achalasia of the cardia. Carcinoma. Cicatricial stricture. Rarely, peptic ulcer of the œsophagus.

**Diverticulum of the Œsophagus** is rare and seldom of importance as a cause of dysphagia.

**Diverticulum of the Pharynx** just above the œsophagus, and often erroneously believed to arise in it, is more common and of considerable clinical importance. Gradual and progressive enlargement ensues, until finally the sac may retain a large amount of food or fluid. When this occurs, the patient complains of extreme dysphagia and pain on swallowing, the difficulty being referred to the neck and a definite bulge or tumour may be visible. If early diagnosis is made by the symptoms and X-rays, before great enlargement of the sac ensues, the results of surgical intervention are good. In late cases emaciation usually occurs from the difficulty in swallowing, and nutrition must be improved by feeding through a catheter into the stomach, after first emptying the sac. Operation may then be considered, but the surgical risks are always serious.

**Plummer-Vinson (Paterson-Kelly) Syndrome.**—An inco-ordination of the reflex act of swallowing at the pharyngo-œsophageal junction, found almost exclusively in middle-aged women suffering from chronic microcytic (hypochromic) anæmia (see p. 464). The treatment is primarily that of the anæmia, and secondarily similar to achalasia of the cardia. In occasional cases, however, passage of the mercury tube may be impossible owing to the presence of webs or bands. Operative treatment is then required.

**Carcinoma of the Œsophagus.**—This occurs as a rule at one of the two narrow parts of the œsophagus—at the level of the bifurcation of the trachea (commoner) or at the cardiac end.

Once the diagnosis is made only palliative treatment is usually possible. Radical surgical treatment, up to the present, has rarely been successful. In the early stages the patient should be encouraged to eat as freely as he can without discomfort, but soon the food must be restricted to semi-solids, and finally only fluids in very limited amounts may reach the stomach. The patient in the later stage is simply starving to death, and the choice must be made between a gastrostomy or the adequate use of morphine. Apart from attempts at radical surgical intervention, efforts have been

made to implant radon seeds through an œsophagoscope, and deep X-ray therapy has also been employed, occasionally with permanent success. Souttar's spiral coiled metal tube may in certain cases be passed through the constricting tumour and left *in situ* until the end, thus enabling some food to be swallowed. No attempt should ever be made to dilate a carcinomatous stricture.

**Achalasia of the Cardia.**—This term is used to describe a condition of obstruction at the lower end of the œsophagus, believed to be due to an inability of the cardiac sphincter to relax (achalasia) rather than to muscular spasm. The older term—cardiospasm—is now less often employed, but the existence of spasm, in some cases at least, is still upheld by competent observers. The condition is chiefly confined to adults of both sexes and is not uncommon.

In the majority of cases diagnosis is easily made by X-rays after swallowing a thin barium meal, but if any doubt exists, the patient should be referred to a specialist for œsophagoscopy. Early diagnosis is of great importance since at that stage permanent cure, or at least permanent amelioration almost amounting to cure, is to be expected. In patients in whom the condition is unrecognized, dilation of the œsophagus above the obstruction may be enormous, and erosion or actual ulceration of the sac may supervene. Passage of any instrument in such cases is difficult and by no means free from danger.

The usual treatment in early cases is both simple and effective, and consists in the repeated passage of a single, or, if absolutely necessary, a series of stout rubber tubes with rounded ends resembling a stomach tube partly filled with mercury to give weight. The series of tubes generally recommended varies from 24 to 34 gauge, but in practice a single tube of 30 gauge generally suffices. The patient at first requires encouragement and actual help in passing the tube down the œsophagus and in allowing it, practically by its own weight, to open and pass the obstruction into the stomach. The tube is left in position for fifteen to twenty minutes, after which it is withdrawn and the patient then finds that food can easily be swallowed. Every patient is gradually, but as a rule without much difficulty, taught to pass the tube on himself or herself. At first the tube may require to be passed before every meal, but eventually its passage is only required daily, weekly, or at irregular intervals. In a few patients it can be dispensed with altogether. In the later stages of treatment the mere passage of the "mercury tube"<sup>1</sup> is sufficient—it may then be withdrawn at once and the meal proceeded with.

In patients in whom the condition is only recognized late, after dilation and elongation of the œsophagus have ensued, treatment is more difficult. The œsophagus should be carefully and repeatedly washed out with normal saline until erosions are healed, and attempts to pass the mercury tube, owing to kinking of the elongated œsophagus, should be undertaken with care. In such patients radiological control with a thin barium meal is advisable. The obstruction is seldom complete, and a fine stream of the barium meal can generally be seen on the X-ray screen demonstrating the course of the channel from œsophagus to stomach.

<sup>1</sup> Inhalation of nitrites before a meal has recently been used with some success in place of the mercury tube. Side-effects with amyl nitrite are unpleasant and nausea or vomiting may ensue. Octyl nitrite (British Drug Houses) is more satisfactory and worth a trial in early cases.

## PEPTIC ULCER OF THE ŒSOPHAGUS

### (*Peptic Œsophagitis*)

Peptic ulcer of the Œsophagus occurs just above the cardiac sphincter, and is identical with the same ulcer in the stomach not only in its structure but also in its important complication of hæmorrhage.

**Acute Peptic Ulcer of the Œsophagus** is a sequel of frequent vomiting and, most commonly in practice, of post-operative vomiting. Fatal hæmatemesis may occur, especially in children.

Treatment is mainly prophylactic and depends largely on efficient post-operative nursing. After severe bouts of vomiting a small amount of an alkaline drink should be given. Healing of an acute ulcer is complete in about ten days, and feeding in suspected cases should be confined to citrated milk given in small amounts frequently repeated.

**Chronic Peptic Ulcer of the Œsophagus** is identical with the chronic ulcer of the stomach and duodenum, but is very much less frequent. It is always found in the lower third, generally just above the sphincter. It may occur when an islet of acid-secreting cells is abnormally sited (*heterotopia*) in the wall of the Œsophagus, but the main ætiological factor is believed to be as described below.

*Chronic Peptic Ulcer in Congenital Short Œsophagus* is now recognized as a clinical entity often missed in the past. In this congenital abnormality the Œsophagus is too short, so that from birth a small part of the stomach is actually in the thorax. Regurgitation into the thoracic pouch can be demonstrated in certain positions of the body, such as lying down or leaning forward, after a barium meal; and the ulcer develops in the Œsophagus close to its termination because the sphincter preventing the entrance of acid from the stomach is inefficient. Stricture may result from scarring round the ulcer, and it is still believed by some that fibrous contraction rather than congenital defect is the main cause of the shortening. When spasm or actual stricture are present, achalasia (p. 529) or early carcinoma may be closely simulated, and Œsophagoscopy may be required to amplify the X-ray picture.

Treatment is best commenced in bed, and in general should be on similar lines to those recommended for gastric and duodenal ulcer. There are certain important differences, however, for the Œsophagus is empty and at rest except during swallowing and acid regurgitation occurs only intermittently in certain positions of the body. Food should be taken only when the patient is sitting up, and instructions given that he must not lie down for at least half an hour afterwards. There is no need for small frequent meals as often recommended in gastric ulcer; on the contrary, adequate soft meals at the usual intervals, and with the precautions mentioned above, allow the Œsophagus maximum rest. A good drink of water should be taken at the end of each meal, and alkalis or olive oil have the same sphere of usefulness as in peptic ulcer elsewhere.

## DISEASES OF THE STOMACH

The treatment of dyspepsia forms a large part of general medical practice, and few individuals go through life without experiencing this symptom at

one time or another. In some instances the cause is obvious, the dyspepsia being related to dietary errors, alcoholic excess, acute infection or some systemic disease, but in many the ætiology is obscure and treatment is difficult. Effective treatment depends on correct diagnosis, and the following simple clinical classification may prove helpful.

**Dyspepsia with Peptic Ulceration.**—Diagnosis in these cases may be easy, or may require the assistance of radiology, gastric analysis and examination of the stools for occult blood. Sometimes the radiologist may be unable to demonstrate an ulcer-crater at the time of examination; but if the clinical picture points strongly to a diagnosis of peptic ulceration, treatment should be carried out just as if the X-ray results had been positive (see p. 535). The group will therefore also include patients who are sometimes labelled as suffering from “duodenitis” after radiological examination.

**Dyspepsia without Peptic Ulceration.**—*With Organic Gastric Disease.*—In this group are included all patients with dyspepsia due to gastritis (p. 534), carcinoma (p. 551) and syphilis of the stomach (p. 554).

*With Extra-Gastric Disease (Reflex Dyspepsia).*—It must be emphasized that dyspepsia may be a prominent symptom of diseases of other organs—e.g., gallstones and biliary disease, pulmonary tuberculosis, anæmia and chronic appendicitis.

*Without Organic Disease.*—A diagnosis of “nervous dyspepsia” has long been correctly recognized, the condition resulting from emotional upsets, business or domestic worries and long hours of work often associated with irregular or “bolted” meals. The active, highly-strung business man and the woman suffering from flatulent dyspepsia of functional origin are typical examples, but there are many others. Conditions of war, both in factories and in the services, have served to add emphasis to the view, which has been quickly gaining ground in recent years, that dyspepsia is a common feature of an underlying psychoneurosis. A careful history will often disclose that these patients, in addition to dyspepsia, complain of undue fatigue, headache, præcordial discomfort and other symptoms associated with an anxiety state. The terms “psychoneurosis” or “anxiety state” unfortunately tend to convey to our patients nowadays an inference or suggestion of personal blame for their illness and so should be avoided in consultations. Nevertheless, they express the medical opinion that the dyspepsia results from the failure of an unstable or inefficient nervous system under conditions of strain.

It is impossible to give an exact idea of the relative frequency of the various types of dyspepsia—organic and functional—in the whole community, since this will vary with the age, sex and conditions of life. Experiences in the three Services during the recent war showed that in men dyspepsia was responsible for about 9 per cent. of admissions to large hospitals. Peptic ulcer accounts for 40 to 50 per cent. of these admissions, but there is still considerable diversity of opinion about the cause of the remainder classified broadly as dyspepsia without peptic ulceration. The main difficulty lies in assessing the relative frequency of “gastritis” and “nervous dyspepsia,” and it is clear that the diagnosis between these depends more on the personal views of the physician than on accurate investigation. To one physician the discovery of abnormal gastric secretion indicates a diagnosis of organic disease; to another, the secretory disorder is only one manifestation of a functional nervous upset. Some are confident in their ability to recognize

gastritis, regarding it as a common disease of obscure ætiology; others believe that certain types of gastritis may be secondary to nervous dysfunction affecting the gastro-intestinal tract. A practical manual of treatment is not the place to embark on a consideration of rival hypotheses, but it is essential for the physician to be aware of the different views so that he may decide with which he agrees, for on his final diagnosis depends the treatment to be adopted. At present it may be said that the importance of psychological factors in dyspepsia is being strongly emphasized, and that a diagnosis of gastritis should be confined to cases showing the fairly typical clinical picture, gastric analysis and radiological appearance. Much of the argument is really sterile and shows a desire to separate the inseparable. In medicine it is no longer possible to regard the terms "organic" and "functional" as mutually exclusive, but rather is it a question of deciding how much of the clinical picture in any one case is due to organic disease and how much to functional disorder.

### NERVOUS DYSPEPSIA

The diagnosis of this condition is made after a complete examination has excluded gross organic disease and by the recognition of a psychological basis for the symptoms. It is necessary that a full examination should be carried out since a neurotic personality confers no immunity against organic disease, and there is no more unfortunate mistake in clinical medicine than failure to recognize a disease such as cancer of the stomach because it occurs in a patient of unstable nervous temperament. On the other hand, the examination should not be unnecessarily prolonged, nor too frequently repeated, in order to avoid strengthening the belief of the patient that he is the victim of some obscure disease which could easily be cured if only his doctor could prescribe the correct medicine.

It is not easy to lay down any scheme of treatment which will prove suitable for all, or even for most, patients with nervous dyspepsia since they differ widely in type and severity. Some cases may be of recent onset with their symptoms clearly attributable to domestic worries or financial difficulty, while others may be of long standing and of obscure causation. The latter group may include those who have been ill for years and who have undergone treatment at the hands of many practitioners, qualified and unqualified. They may even have been subjected to surgical operations. The following plan of treatment, however, may be modified according to the particular needs of the patient.

**Psychotherapy.**—The first point to be decided is whether the practitioner should undertake the psychological treatment of the case by himself or whether he should seek the assistance of a specialist in psychology. Before coming to a decision he should read the section on "The Scope and Limitations of Psychotherapy in General Practice" (p. 913). Assuming that the case is not one requiring specialist help, the first step is to take a full history, encouraging the patient to talk of his fears and anxieties, his hopes and desires, with the object of discovering what is faulty in his reaction to his environment. In the more simple examples of nervous dyspepsia—and it is only in these that the practitioner should attempt psychotherapy by himself—the cause of the emotional disorder may now become apparent, perhaps

arising out of some business or domestic worries. Next, the disturbances of bodily function which follow emotion should be explained to the patient. It is not difficult to find examples: tachycardia and diarrhoea arising out of fear; the choking sensation caused by grief; horror as a cause of syncope; vomiting, anorexia and epigastric discomfort as features of anxiety; and many others will suggest themselves and will be understood by the patient. These are explained as natural occurrences in normal people, the neurotic person differing only in that his symptoms are not transient but persistent. Since the patient has now been made aware that symptoms of bodily disorder can be produced by emotional upset he may be ready to accept this explanation of his complaint, and willing to regard himself as a worried but not a sick man. Simple explanation in this way may suffice to produce an improvement, but even if some relief is not secured, and in many cases it is not, the patient may be able to face his difficulties without the handicap of believing that he is the subject of an incurable disease, for the treatment of which his doctor has nothing to offer except perhaps the unwelcome assurance that it is "only nerves." It is customary to advise these patients to avoid all worry and excitement, advice which the majority find impossible to follow even in the absence of any adequate reason for worry. Furthermore, when a real cause of worry exists it may be of such a nature that it simply cannot be avoided, for example in a woman whose husband is dying from pulmonary tuberculosis. In such cases a sympathetic explanation of the cause of the symptoms is the most that can be done.

**Drugs.**—It is a feature of nervous dyspepsia that medicines give little permanent relief, and innumerable prescriptions of alkalis, proprietary and otherwise, may already have been tried. If it is obvious that the patient expects some medicine to be prescribed, there is no objection to the temporary use of a placebo as an aid to psychotherapy, and in some chronic cases of poor intelligence the faith excited by a bottle of medicine may serve to keep the patient in reasonable comfort when psychological treatment has completely failed. In general, the only drugs which are of real value in nervous dyspepsia are those with a sedative action, and the use of phenobarbitone in half-grain doses, twice or thrice daily, is of great assistance, especially when insomnia exists.

**Diet.**—As is the case with drugs, the patient may expect a diet to be prescribed, and there can be little objection to dietary treatment in the initial stages. The diet for peptic ulcer (pp. 538, 549) is quite suitable, but the additions should be made more rapidly than with peptic ulceration, and the patient should be taking a normal diet within a few weeks. It is of therapeutic importance to note that dyspeptic patients often come to believe that their symptoms are due to eating certain foods and thereupon, acting on medical advice or of their own accord, they begin to limit their diet. When this fails, further restrictions may be imposed until finally their psychoneurosis and dyspepsia are further complicated by chronic malnutrition. In rare cases clinical evidence of vitamin deficiency, such as scurvy and beriberi, may appear; but as a rule the signs of chronic ill-health are simply exaggerated and continued. True intolerance to certain foods does exist, although it is uncommon, and the patient may be permitted to omit certain articles from his diet provided that in so doing he does not deprive himself of dietary essentials; but drastic dietary restriction must not be permitted.

### GASTRITIS

**Acute Gastritis.**—This may result from the swallowing of corrosive poisons, the stomach sharing in the damage done to the œsophagus. Apart from the administration of the antidote, if known, no other treatment is possible.

Acute gastritis of lesser severity (catarrhal gastritis) is exceedingly frequent and due to a great variety of causes. Common varieties in practice are the result of indiscretions in food or alcoholic drinks; but contaminated food, "chill" (especially in the tropics) and scarlet fever in its acute stage may also induce very acute gastric catarrh. In any variety the inflammation may spread downwards to cause acute gastro-enteritis. The cardinal symptom of acute gastritis is vomiting, and when enteritis is superadded diarrhœa also supervenes.

The treatment of acute catarrhal gastritis is best considered as part of gastro-enteritis, the treatment of which is dealt with under the heading of Diarrhœa (p. 557).

**Chronic Gastritis.**—This was formerly a common diagnosis. Thereafter came a time when, apart from its recognized existence in habitual alcoholics, the conception of chronic gastritis fell into disrepute and the use of the term was frowned on in sick reports. Now, again, chiefly as a result of the pathological work of Faber, of Copenhagen, and of developments in radiological and gastroscopic technique, chronic gastritis has come into its own, and is properly regarded, when correctly diagnosed, as an important and by no means infrequent disease. Accurate diagnosis is essential, but, when made, the use of the term is entirely justified.

It is important to treat this disease in as early a stage as possible, not only for the immediate disabilities which arise but still more for the serious consequences, such as carcinoma, which may possibly result from it. Much of the treatment is essentially prophylactic and consists in the removal of such well-known causes as alcoholism, oral sepsis (especially pyorrhœa) and deficient mastication of food (from bad habits or lack of teeth). Excessive use of strong tea, coffee and tobacco have all been blamed as causes, but proof is difficult. The cardinal symptoms and signs of an established case which demand treatment are:—

1. Vomiting, especially in the morning and associated always with an excessive secretion of mucus into the stomach.
2. Diminution or frequently complete absence of hydrochloric acid in the gastric juice. (In the rare hypertrophic variety of gastritis, hyperacidity occurs.)

The prime causes favouring continuation of the disease having been removed, the first essential in treatment is gastric lavage (p. 555) carried out always before breakfast and in the severer cases at intervals during the day, before meals. Warm water is in many cases quite adequate to wash out the stomach; but if mucus is present in large amount, 1 to 4 drachms (3.6 to 14.4 c.c.) of hydrogen peroxide (10 volumes) is added to 1 pint of warm water. This helps mechanically to "bubble" the mucus away from the gastric mucosa. Treatment by lavage is continued until improvement is manifest, when its use can be gradually discontinued. If lavage is for any reason impossible, the next best substitute is the administration of a teaspoonful or more of sodium bicarbonate in a tumblerful of warm water in the morning, and again before meals throughout the day.

Hydrochloric acid is so commonly greatly diminished or absent in an untreated case of chronic gastritis that some effort is generally made to remedy the deficiency. For this purpose 1 to 2 drachms (3.6 to 7.2 c.c.) of acid. hydrochlor. dil. should be added to a tumblerful of lemonade or orangeade with instructions to drink this as a beverage with each main meal. Since, however, the amount of acid normally secreted after each meal is equivalent to about 7 drachms (25 c.c.) of dilute hydrochloric acid, B.P., and since this amount could not be taken without severe irritation to the throat, the prescription of acid as suggested cannot be regarded as an adequate form of replacement therapy. Further, in some patients pain results and the dosage advised above must be reduced. It is known that after gastric lavage for some weeks the secretion of hydrochloric acid frequently returns in adequate amount.

Anorexia is common in chronic gastritis, especially in the morning when there is a great excess of mucus in the stomach. Later in the day the appetite generally improves. Bad dietary habits are common in these patients, and especially in alcoholic gastritis. The prescribed diet should be arranged so that attractive, small meals are provided at frequent intervals, bland in character and adequate in calories, minerals and vitamins. Most textbooks of dietetics give examples of special diets for use in gastritis, but this is unnecessary as the diet for peptic ulcer (p. 549) can easily be modified to suit. In order to stimulate the gastric secretion, soups and meat extracts, such as Bovril, should be added and the inhibitory action of fats partly avoided by reducing the quantity of butter to one ounce daily. Since it has been suggested that achlorhydria may prevent the proper utilization of the vitamin B complex, and since achlorhydria may appear in vitamin B deficiency, it is usual to prescribe Marmite to be taken in soup, as a beverage or in sandwiches. Alcohol must be strictly forbidden and smoking stopped, or restricted to after meals. A bitter tonic containing 5 to 10 minims (0.3 to 0.6 c.c.) of tincture of nux vomica and 30 to 60 minims (1.7 to 3.5 c.c.) of compound tincture of gentian, taken before meals, may be helpful.

There is no doubt whatever that for patients able to afford it spa treatment is of great assistance for many reasons. Abundance of a mildly aperient spa water corrects the almost invariable constipation and washes out the stomach, while the regular spa régime should enable patients to amend their habits. When such treatment is impossible, bottled spa water may be taken at home, and sodium phosphate, 1 drachm (3.9 gm.) in  $\frac{1}{2}$  pint of water, is a substitute for the well-known Carlsbad water.

The patient suffering from chronic gastritis is likely to be irritable, depressed and difficult to handle, and a great deal of common-sense psychological treatment may be required.

## GASTRIC AND DUODENAL ULCER

### *(Peptic Ulcer)*

Chronic peptic ulcer is found (1) on the lesser curvature of the stomach; (2) near the pylorus (pyloric antrum); and (3) in the first inch of the duodenum (duodenal ulcer). Other parts of the stomach wall are less frequently involved, or the ulcers may be multiple.



The treatment of a straightforward case of chronic peptic ulcer is essentially the same, whatever its position. Differences arise in long-standing cases only because each of the varying anatomical positions tends to be associated with special complications. Duodenal ulcer is especially liable to lead to organic pyloric stenosis; ulcer of the lesser curvature to deep penetration into the pancreas or to hour-glass stomach; while ulcer of the pyloric antrum has a well-known tendency, unlike ulcers on other sites, to become malignant. Any peptic ulcer may perforate, when the immediate treatment is surgical.

Formerly it was the custom to regard the treatment of peptic ulcer as a problem in the neutralization of hydrochloric acid, but recent work has shown that this simple hypothesis is unsatisfactory. It is true that duodenal ulcer is generally associated with hyperchlorhydria, but this is by no means invariable, and a diagnosis of duodenal ulcer is compatible with a secretion of acid within normal limits. In gastric ulcer an excess of hydrochloric acid is an inconstant or even unusual feature. Furthermore, it has been shown that healing of the ulcer may take place in the presence of uncontrolled hyperchlorhydria; but the strongest evidence that neutralization of hydrochloric acid is not essential in the treatment of peptic ulceration comes from many recent studies on the gastric secretion in patients undergoing treatment. It has been conclusively shown that methods of treatment which were introduced to control acid secretion are quite ineffective for this purpose. For example, hourly or two-hourly feeds of milk or milky foods, combined with doses of olive oil, alkalis and belladonna (as recommended by Hurst), do not control gastric acidity over twenty-four-hour periods any better than diets consisting of four meals a day. In spite of failure to control acid secretion the healing of the ulcer is not interrupted.

These results indicate that the importance of the acid factor in the treatment of peptic ulcer has been exaggerated, and some physicians have adopted the view that mental and physical rest are of more importance in promoting healing than treatment with diet and alkalis as in the former routine manner. One serious objection to this attitude is that peptic ulceration only occurs in those areas exposed to the action of acid gastric juice, in the stomach and duodenum, in the jejunum after gastro-enterostomy and in the œsophagus and Meckel's diverticulum where heterotopic gastric mucous membrane may occasionally be found. Peptic ulceration is very rarely seen in the absence of free hydrochloric acid, and the clinical dictum of "no acid, no ulcer" is true for the vast majority of cases. With these points in mind, and without forgetting the importance of securing mental and physical rest for the patient, it is impossible to ignore the influence of acid gastric juice in producing peptic ulceration. Similarly, although the use of frequent feeding, alkali and belladonna is ineffective in controlling the secretion of acid, this method of treatment cannot be entirely discounted since it has been shown capable of giving good results in practice. In our present state of ignorance concerning the causation of ulcer-pain (it is not due to hyperchlorhydria alone, since it is relieved by treatment which does not control the acidity), it is difficult to explain why these good results are obtained, but it is probable that they are due to the effects of the treatment on gastric motility and spasm. According to this view the pain is due to some disturbance of motility, either spasm or increase in muscular tension, and the presence of food or the evolution of gas from

alkali, by increasing the volume of the stomach contents, produces an adaptive relaxation of the gastric walls. The entrance of food or gas into the duodenal cap may relieve spasm in cases of duodenal ulcer by a similar mechanism. Since it is certain that emotion can cause disordered gastric motility, this hypothesis will serve to explain the improvement which occurs in patients with peptic ulceration who are given mental and physical rest by confining them to bed without any other form of treatment.

With the above general principles in mind, the details of treatment may now be considered.

**Initial Management.**—The first point to decide, after the diagnosis has been made, is whether treatment should be begun with the patient in bed. The writers have no doubt that this is the best method, and that if the patient is kept absolutely at rest for four to six weeks the time of healing may be greatly shortened. It has been truly said that if a patient suffering from uncomplicated peptic ulcer is not entirely relieved of his symptoms after a few days in bed the diagnosis is probably wrong. This fact must be remembered, and the patient informed that although his symptoms have disappeared the ulcer remains unhealed.

In spite of this ideal it must be stated that in existing circumstances many ulcer patients are treated from the outset as "out-patients" at our hospitals or "while at work" in private practice. This is often quite successful if the patient co-operates and no complications supervene. Too few hospital beds exist for the prolonged treatment of this common disease, and even in private practice it may be unwise to add to other worries the fear of loss of employment by insisting on several weeks in bed.

Thus, while an initial period of rest in bed is the ideal (and must always take first place in the doctor's mind), circumstances may reasonably modify the advice given.

Three other factors also arise at the very outset of treatment—the psychology of the patient, the problem of smoking and the condition of the teeth.

Many attempts have been made within recent years to define an "ulcer personality" in psychological terms, particularly in considering duodenal ulcer, and some measure of success has been attained. The defect has been expressed as one of hypermotility, hyperirritability and hypersensitivity not only of the duodenum but of the patient himself, and it is true that in many cases a careful history will show the onset of the illness to have followed, or to have been associated with, some emotional upset. Anxiety caused by financial difficulties, illness in a relative, fear of dismissal from employment, or following promotion to a post of greater responsibility, not uncommonly precedes the onset of symptoms, and emotion caused by frustration or injustice, real or imagined, has also been blamed. The effect of nervous tension on peptic ulceration was strikingly shown by the increase in the number of cases of perforated peptic ulcer during the time when severe air raids were common in this country; but under ordinary circumstances the ill effects of nervous tension on gastric function are to be seen in the frequency of dyspepsia and peptic ulcer in certain occupations, such as bus driving, especially when long hours are worked. Failure on the part of the patient to adjust himself to new and possibly uncongenial surroundings is also thought to be of importance in initiating ulcer dyspepsia and may play a part in the breakdown of ulcer patients in the services.

This view that the ulcer patient is of a certain psychological type has excited much interest and is accepted by most as being of ætiological significance. It is necessary, however, to retain a balanced judgment, and remember that other factors, such as the season of the year, the presence of infection, irregular and hurried meals, are also of importance, and that the recognition of an "ulcer personality" does not resolve the mystery of the cause of peptic ulceration. Nevertheless, from the standpoint of therapeutics, the conception of a psychological factor is of great value since it provides an indication for positive treatment. The patient may be unable to live a more placid life when advised to do so, but by persevering he may be able to correct his more obvious faults. It is to be noted that the patient is generally quite unaware of the possibility of any connection between emotional factors and his symptoms, but when the question is discussed he is frequently ready to admit that they may be of importance in this respect. Once he has recognized the association between his emotions and his pain he is more likely to remain well for longer periods than if his attention is solely directed towards dietary treatment and the necessity for taking alkalis.

Although there is no proof that smoking, even in excess, is a direct ætiological factor in peptic ulcer, there is no doubt that nicotine acts as a gastric irritant which, especially on an empty stomach, must be harmful. The advice to be tendered to the patient at the end of treatment for peptic ulcer is dealt with subsequently, but in the earlier stages the writers have no doubt that smoking should be absolutely forbidden.

Many patients suffering from peptic ulcer are found on examination to have dental caries, pyorrhœa, or an inadequate number of teeth. The front teeth alone may be present, and the molars, so essential for mastication, may have disappeared and may not have been replaced by dentures. It is obviously sound to start treatment with a reasonably clean mouth and with provision made for adequate mastication in future.

**Dietetic Treatment of Peptic Ulcer.**—Great care and attention have always been paid in modern medicine to dietetics in peptic ulcer, but since our knowledge is constantly increasing, no finality has been reached, and at the present time our views are in the process of change. The earlier dietetic treatments were concerned with two things only—efficient neutralization of hydrochloric acid and prevention of irritation of the healing ulcer. In the acute stages, and particularly after a recent hæmorrhage, it is now realized that too little attention was paid to the provision of sufficient calories and vitamins to maintain health. In the past, as we now know, in connection with this and other diseases, the disease rather than the patient was chiefly considered. However, certain principles are common to most standard systems of dietary treatment and are tabulated here:—

1. The omission or limitation of substances which stimulate gastric secretion such as highly seasoned foods, soups and other foodstuffs containing extractives.

2. The omission of coarse substances such as raw vegetables and the pips and skins of fruit, and the use of sieved vegetables so as to avoid mechanical irritation of the ulcer.

3. The omission of gastric irritants such as strong tea, coffee and alcohol.

4. The inclusion of bland foods such as milk and eggs, and the adequate consumption of butter, margarine and cream so that gastric motility is slowed and gastric secretion diminished.

5. The taking of small meals at frequent intervals so that pain is relieved and undue distension of the stomach avoided. Some patients with peptic ulcer complain of pain solely, or chiefly, after the largest meal in the day.

6. The diet must be of sufficient caloric value and contain the necessary vitamins. The older dietary systems often provided inadequate amounts of vitamin C, but this defect has been rectified nowadays by advising the use of orange juice. In times of rationing, one 50 gm. tablet of ascorbic acid may be substituted for the orange juice.

Although these principles are common to most diets used for peptic ulcer, there is no general agreement on the composition of the diet to be used at the beginning of treatment. Within recent years the tendency has been to prescribe a diet which approaches that of a normal individual (modified so as to conform with the general principles), even in the acute stage of the illness. Details of a specimen diet are given on p. 549. The more rigid dietary systems restrict the patient to milk and milk foods during the first few weeks of treatment, and it is not until the end of this period that a more generous diet is allowed.

The Hurst régime, developed by the late Sir Arthur Hurst from the Sippy diet used in the United States, is an elaborate combined system of food and drugs devised with the aim of achieving continuous neutralization of hydrochloric acid. As has been indicated, however, this objective is not really attainable in practice, nor is it essential for healing. Moreover, the method requires hourly nursing attention to the patient, which in present circumstances is virtually impossible. The writers, therefore, no longer advise it, and believe that just as good results can be obtained by simpler dietetic methods. We wish to state, however, that the Hurst régime successfully withstood the test of long practical experience in Britain, and when it could be carried out completely the end-results were satisfactory.

**The Post-Ulcer Period.**—The healing of a chronic peptic ulcer is a long process. Gastrosopic examination has shown that many ulcers, thought to be healed and no longer showing an ulcer niche on radiological examination, are in reality smaller but still active. A gastric ulcer may be covered by epithelium in seven to eight weeks, but sometimes not for five to six months. A thin covering of epithelium, however, is only the first stage of healing, and unless treatment is strict it may easily break down. Strict treatment is therefore essential for at least six months or the cure may only be temporary. The scars of old peptic ulcers in the post-mortem room show that complete and permanent healing does take place, but in the majority of cases peptic ulcer should be regarded as a recurring disease and the principles learned by the patient during the active period of treatment should be continued for life. For example, the patient should know the general principles of dietary treatment, the necessity for thorough mastication of food and for regular meal hours, the value of physical and psychological rest, the ill effects of too long hours of work and of nervous strain. The importance of this long-term policy in the treatment of peptic ulcer cannot be too strongly emphasized if chronic ill-health is to be avoided.

The problems of alcohol and tobacco arise again in the post-ulcer period. Strong alcoholic drinks of all kinds, and particularly when taken on an empty stomach, should be avoided, but there is no real objection to more dilute spirits and wines taken along with meals. Smoking on an empty stomach must also be strictly forbidden. Some patients find it possible to adhere to the rule of smoking only after meals and at no other time. Others prefer to give up smoking for life, and, as the habit has been stopped during the early stages of treatment, the final decision is less difficult for the patient.

**Drugs in the Treatment of Peptic Ulcer.**—*Alkalis* are the most used and probably the most abused remedies in the treatment of real or supposed peptic ulcer. They give immediate symptomatic relief in most forms of "acid dyspepsia," and the amount of alkali powders and tablets of proprietary brands purchased by the public and used without medical advice is incredibly large. When used in excess, or even in moderate amount by susceptible individuals, severe alkalosis (p. 546) may result, and it is extraordinary that this serious complication is comparatively seldom encountered in ordinary practice. When correctly used, alkalis are undoubtedly of value in the symptomatic treatment of peptic ulcer.

A number of alkalis are available which differ somewhat in their action, but there is no general agreement as to which should be used. All carbonates liberate  $\text{CO}_2$  in the presence of hydrochloric acid, and this property may be thought disadvantageous as distressing gaseous distension of the stomach may follow. In practice, however, the majority of patients do not complain of distension since it is followed by belching which relieves the pain. Sodium bicarbonate and magnesium oxide may render the gastric juice alkaline in reaction, and when this occurs a great secondary secretion of acid is provoked. These alkalis are in fact the most powerful stimulants of gastric secretion known, with the exception of histamine; but if they are given in doses insufficient to produce complete neutralization the secondary stimulation of acid is unlikely to occur. Most other alkalis, such as calcium carbonate, sodium and potassium citrates, and tribasic calcium and magnesium phosphates, produce a neutral solution and do not cause this secondary secretion of acid. Bismuth oxycarbonate has a negligible antacid action in therapeutic doses, and it is equally useless as an astringent; neither does it form a protective coat to the ulcer as traditionally believed; but it is still used in the belief that it exerts a sedative action on the gastric mucosa although experimental evidence is lacking. The risk of producing alkalosis (p. 546) is diminished by the use of the tribasic phosphates, and this danger is absent when aluminium hydroxide or magnesium trisilicate are used. The last two antacids are not so widely used as the others and there is no proof that they are more valuable in ordinary medical practice, but they should be tried in patients who do not obtain relief with the alkalis which have been described.

A common type of prescription is as follows:—

R $\bar{7}$	Calc. Carb.	.	.	.	.	} $\bar{a}\bar{a}$ 1 part
	Mag. Carb. Pond.	.	.	.	.	
	Bism. Carb.	.	.	.	.	

Mix and make a powder. Send 10 oz. (310 gm.)

Sig.—One teaspoonful or more, in water or milk, as directed.

Since the calcium salt has a constipating, and the magnesium salt a laxative action, the quantities used may require to be adjusted so as to avoid excessive action in either direction.

One of the writers has found tribasic magnesium phosphate (one teaspoonful after each meal and two at night) very useful. If too aperient, this may be combined with tribasic calcium phosphate in varying amount to suit the individual case.

Apart from the alkalis, only two other remedies are said to play any real part in the control of gastric secretion, namely, belladonna (or atropine) and olive oil.

*Atropine.*—It was claimed that belladonna, or its alkaloid atropine, diminished or even abolished gastric secretion, but this has been disproved at least for therapeutic doses. They are probably of value, however, for the relief of pylorospasm, although they should be used with care in ambulant patients, and particularly in those who may drive motor cars. The susceptibility of patients, and the effects on the eyes, vary considerably.

*Olive Oil* (or arachis oil), on the other hand, can do no possible harm, and is frequently given to patients suffering from peptic ulcer with great advantage. When taken on an empty stomach it diminishes the flow of gastric juice, relieves flatulence and is a valuable source of food. The value of olive oil is being more and more appreciated and the writers wish particularly to emphasize its importance.

*Sedatives.*—Phenobarbitone,  $\frac{1}{2}$  gr. (0.03 gm.) three times a day, is of the greatest assistance in securing physical and mental rest for the patient, and is a useful aid in what may be termed the psychological treatment of the case.

*Iron.*—Anæmia as a result of slow leakage from an ulcer is extremely common and is treated with iron (p. 470).

**Surgical Operation** in relation to the treatment of peptic ulcer is discussed under Hæmatemesis and Melæna (see below), Pyloric Stenosis and Hour-glass Stomach (p. 546). The special problems which may follow a primary operation for ulcer are referred to on p. 548.

#### TREATMENT OF COMPLICATIONS

The complications of peptic ulcer are many and the treatment required for each must be considered in detail.

**Hæmatemesis and Melæna.**—Bleeding from the stomach may be followed by vomiting (hæmatemesis) or melæna (bleeding from the bowel), and each has the same significance when the origin of the bleeding is a peptic ulcer. The clinical problems of bleeding from dilated œsophageal veins, in portal cirrhosis and splenic anæmia, have already been referred to (p. 496). In some cases the origin of a sudden hæmatemesis may be impossible to trace, but the immediate treatment at least is the same. A grossly enlarged spleen or obvious signs of portal back pressure should not escape clinical observation.

Hæmorrhage from a peptic ulcer varies greatly in amount and frequently a poor estimate is made by the patient or his friends. It is best, therefore, to rely chiefly on the clinical features. Moreover, it must be remembered that an initial small hæmorrhage may be followed soon after by a very severe one. A single large hæmorrhage from a peptic ulcer is seldom fatal; the notoriously dangerous cases are those in which bleeding is continued or, more commonly, is repeated in attacks at short intervals within a few days.

*Immediate Treatment.*—The patient who has a severe hæmatemesis is pallid, anxious and in a state of shock. An injection of  $\frac{1}{4}$  gr. (16 mg.) morphine hydrochloride with  $\frac{1}{100}$  gr. (0.6 mg.) atropine sulphate should be given at once and the patient put to bed. The room is kept quiet and semi-darkened, the patient's head is kept low, and the foot of the bed may be raised. A hot-water bottle, carefully covered, is applied to the feet. A nurse should watch the pulse-rate, which should be recorded every half-hour for at least six hours (preferably for twelve hours) and at hourly intervals thereafter. Charts taken in our wards show clearly that this is by far the most important routine clinical observation to be made, and its

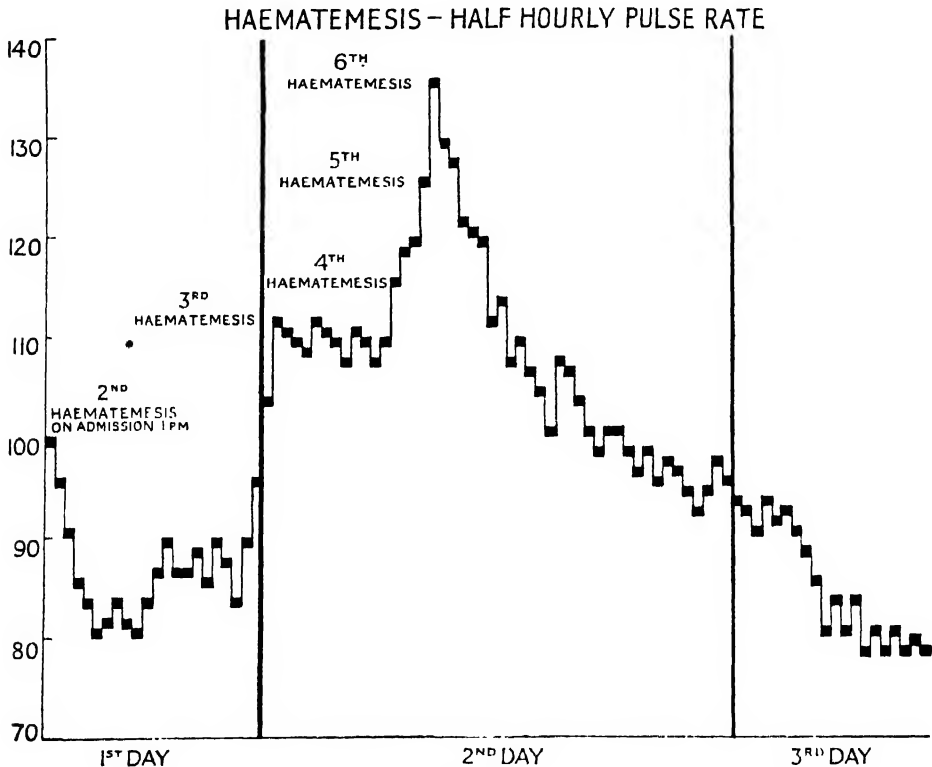


FIG. 4

value cannot be over-emphasized. A steady fall in the pulse-rate indicates that all is going well, whereas a sudden rise gives immediate warning that further bleeding is taking place. If restlessness supervenes it may be necessary to give a further dose of morphine and atropine.

During the first twelve hours the physician takes stock of the event, amplifies the history, and lays his plans for emergencies and for subsequent treatment.

*Subsequent Treatment.*—The chief emergency the physician faces is the repetition of bleeding which may end in death. After an initial hæmorrhage, further bleeding is by no means infrequent during the same day and may occur at any time up to seven days or thereabouts after the initial attack; thereafter the risk is very greatly lessened. Recognition of repeated hæmorrhage is not always easy. It is true that when the hæmoglobin level falls

steadily over a period of days it is generally the result of continued bleeding; but estimation of the hæmoglobin level at the time of the hæmorrhage may be misleading. When a sudden hæmorrhage takes place the loss affects blood plasma and cells equally, so that the percentage of hæmoglobin is unaltered, although the total blood volume has been reduced, and it is not until a variable time after the bleeding that the hæmoglobin level falls by dilution. Melæna, which follows every hæmatemesis, also gives little immediate help as regards the continuation or repetition of hæmorrhage. Tarry stools may be produced by less than half a pint of blood swallowed under experimental conditions, and they may persist for as long as five days. The diagnosis of severe or continued bleeding therefore rests mainly on clinical observation and involves consideration of the quantity of blood vomited or passed *per rectum*, the presence of collapse, restlessness and air-hunger, and the record of the pulse-rate and blood pressure over a period of time. Estimation of the blood urea is helpful in the assessment of a case, as the height of the rise is closely correlated with the severity of the hæmorrhage, and any case in which the blood urea rises much above 75 mg. per cent. must be regarded as severe.

*Diet after Hæmatemesis and Melæna.*—There are three schools of thought regarding diet in hæmatemesis: the first allows nothing to be given by the mouth during the first twenty-four to forty-eight hours or until hæmorrhage has ceased; the second permits the patient to be fed immediately after the bleeding; and the third, which is really a modification of the second, allows fluids to be given by the mouth during the first two days. The principle of initial starvation was for long almost universally accepted. In this form of treatment the patient is permitted to rinse his mouth with water, but otherwise nothing is given by the mouth until the second or third day, when he is allowed sips of water, half-normal saline, whey or citrated milk, the quantities being gradually increased until 5 to 7 oz. are being taken every three hours. Some attempt to relieve the dehydration is made by giving 8 oz. of normal saline by the rectum every four hours; but as a sick person requires in the neighbourhood of 3½ litres of fluid a day, without taking into account the fluid lost in the vomit, dehydration inevitably develops. In spite of this, and although the treatment caused patients much suffering from thirst, the principle was not seriously challenged until 1933, when Meulengracht published the results of treatment by immediate feeding and showed that the mortality was less than with initial starvation. Meulengracht's results have been generally confirmed in this country, and the modification of his diet recommended by Witts (p. 550) has been widely adopted. This diet provides between 2,500 and 3,500 calories a day with adequate quantities of ascorbic acid and the vitamin B complex, and the use of concentrates of vitamins A and D is also recommended. The fluid content of the diet averages 2,750 c.c., and allowing for the water of oxidation the patient is probably provided with some 3½ litres of fluid a day. Witts advises the use of iron from the start, but most physicians prefer to give this only after frank hæmorrhage has definitely ceased. Purgatives are not allowed, and enemata are not used until after the fifth day.

We can confirm the good results obtained with treatment by immediate feeding, and it seems fairly certain that this method does reduce the number of deaths from hæmatemesis. Fatalities from hæmatemesis are bound to occur whatever treatment be adopted, and a study of the pathology in



fatal cases makes it clear that the presence or absence of food in the stomach does not influence such calamities. When nausea or continued vomiting is present the patient may be unable to take the diet. If fluids alone are given by mouth the first of these difficulties may be overcome—the problem of continued vomiting will be dealt with later. We believe that the chief advantage of treatment by immediate feeding is the provision of an adequate fluid intake and prevention of dehydration, and so the fluid part of the diet is more important than the solid; but it is an added advantage if the patient is capable of taking the whole diet and so maintaining his intake of calories, minerals and vitamins. Therefore, in our opinion, the question of whether both solids and fluids should be given by mouth from the beginning, or fluids alone, can only be decided by treating each patient as an individual problem.

*Continued Vomiting.*—In a few cases the vomiting of “coffee ground” material continues and delays or prevents the commencement of feeding. If the vomiting persists life is endangered and a difficult problem is created. Atropine in doses of  $\frac{1}{100}$  to  $\frac{1}{50}$  gr. (0.6 to 0.3 mg.) has been recommended but is ineffective. In a serious case the doctor is advised to take the risk of passing a stomach tube and carefully emptying the stomach, using for the lavage a few ounces of warm water several times repeated. Only the most gentle suction should be employed and the stomach tube should be of the large type. The danger of dislodging clot from the bleeding vessel is obvious, but the risk may have to be taken.

*Parenteral Fluids.*—There are two complications which may call for the administration of fluids parenterally after severe or repeated hæmatemesis—dehydration and post-hæmorrhagic shock. The first is the more common and its treatment is relatively simple, fluids being given rectally, intravenously or subcutaneously. Details of the methods will be found in the section on Technical Procedures (p. 923). Post-hæmorrhagic shock is more serious, being the actual cause of death in most fatal cases of hæmatemesis, and the only effective treatment is to restore the blood volume to normal. This can only be achieved by transfusion of blood, plasma or serum, and since there has been a loss of red blood corpuscles, blood is to be preferred. Treatment of this complication therefore involves a consideration of the indications for blood transfusion.

*Blood Transfusion.*—The main indication for blood transfusion is the recognition of post-hæmorrhagic shock, preferably in its early stages. This requires good clinical judgment, and there is some difference of opinion regarding the indications for blood transfusion in the treatment of hæmatemesis. The needs of the case must be judged on its merits and against a background of clinical experience, but the following signs are generally recognized as indicating the necessity for blood transfusion: a hæmoglobin level of less than 40 per cent.; a systolic blood pressure of less than 90 mm. Hg.; a blood urea level of more than 100 mg. per cent. and a pulse-rate of more than 140 per minute. The transfusion should be continued until these unfavourable signs have disappeared, and so it is impossible to say how much blood should be given in any one case. The usual quantity required is between 1,000 c.c. and 1,500 c.c., but some patients may require as much as 6,000 c.c. It has been stated that blood transfusion may excite further hæmorrhage by causing a rise in blood pressure, and this danger might occur if large quantities of blood were introduced rapidly into the circulation. This, however, should never be done, and when the blood is

given slowly (30 to 40 drops a minute) the blood pressure does not rise suddenly and there is no risk of causing further bleeding in this way. The technique of continuous blood transfusion by means of a drip apparatus is given on p. 937.

*The Use of Hæmostatics.*—No form of hæmostatic agent, either introduced into the stomach itself or parenterally in an attempt to increase blood coagulation, has in practice proved of any real value. Calcium, so often given in the past, is useless.

*The Problem of Operation.*—There has been much argument about the place of surgery in the treatment of hæmatemesis, but the following may be taken as the opinion of most authorities. If all cases of hæmatemesis are considered, the mortality from medical treatment is very small; according to some observers it may be less than 2 per cent. Therefore, in an unselected series of cases surgery cannot be expected to lower the mortality when the risks of surgical operation are considered. On the other hand, if only the most severe examples of hæmatemesis are included, the mortality may be 25 per cent. or more with medical treatment, and the point at issue is whether this figure can be improved. It is difficult to answer this question, as only in large hospitals is there a sufficient number of cases of this type, and there is no generally accepted criterion of what constitutes *severe* hæmatemesis. The chief difficulty is to decide in any individual case whether death is likely to occur with medical treatment and whether surgical intervention is likely to be successful. At present there is no way of predicting the failure of medical treatment other than by observing a progressive deterioration in the condition of the patient despite efficient medical treatment, and this often means that by the time surgical opinion is sought the patient is critically ill and a poor risk. The age of the patient must always be taken into account in making a decision, as death from hæmatemesis is rare under the age of forty. Apart from technical difficulties which may be formidable and are not considered here, the success of the operation depends on the control of a localized bleeding point such as is found in a chronic ulcer.

If the hæmorrhage is coming from a superficial erosion of the mucous membrane there will be no external indication of its site, and even if the stomach is opened no obvious bleeding point may be found. By excluding all patients who have only a short history of gastric pain, the risk of advising operation in a superficial erosion is greatly diminished. The indications for serious consideration of surgery may therefore be briefly summed up as—continued bleeding showing no sign of stopping despite efficient medical treatment, including repeated transfusions of blood, in a patient over forty years of age, with a long gastric history strongly suggesting a chronic peptic ulcer.

If surgery be decided upon, transfusion of large quantities of blood may be required before, during and after the operation. At best the risk is considerable, and operation should only be undertaken when the fullest facilities are available.

*Anæmia following Hæmatemesis and Melæna.*—This is inevitable in all cases and, moreover, the hæmoglobin is lost to the body by the hæmorrhage. To enable the bone-marrow to react rapidly, iron must therefore be supplied in full doses as in any other type of hypochromic anæmia (p. 470). There is no contraindication to the commencement of adequate iron therapy as soon as possible after hæmatemesis has ceased.

**Perforation.**—This may occur either in an acute or chronic peptic ulcer, but particularly in the duodenal variety. The immediate treatment is surgical, and the success of surgery is remarkable even after perforation has existed for a number of hours. The treatment of perigastric adhesions and abscess is not within the scope of this book. The only aspect of perforation of special interest to the physician is when slow leaking perforation occurs, with strictly localized peritonitis and insufficient general signs to demand immediate operation. Such patients should be given morphine and otherwise treated with the same care as if hæmatemesis had occurred.

**Pylorospasm and Organic Pyloric Stenosis.**—*Spasm.*—The usual evacuation of the stomach contents may be prevented by spasm of the pylorus, which occurs at some time in almost every case of peptic ulcer situated close to the pylorus, whether on the gastric or duodenal side. The ulcer by reflex irritation stimulates the pyloric sphincter, but it must be remembered that the same condition occurs in association with many other diseases apart from the stomach, for example, gall-stones and chronic appendicitis. The main effects of pylorospasm are pain and flatulence, and the problems of treatment by belladonna and olive oil have already been discussed.

*Stenosis.*—Organic pyloric stenosis, due to actual cicatrization of an ulcer, presents an entirely different problem. Even here, however, correct diagnosis may not be easy and a radiological report fallacious, since organic constriction due to scarring may be closely simulated by intense pylorospasm or by a combination of œdema and spasm. The effect of medical treatment of pylorospasm, by belladonna or atropine, should always first be tried. Cases of long standing, with enormous dilatation of the stomach, copious vomiting, and active fermentation of the gastric contents are not often seen nowadays, since diagnosis by X-ray examination is so easy. The clinical evidence of active peristalsis, observed only when the stomach contains food or fluid, is also unmistakable. The treatment is always surgical and gastro-enterostomy is generally performed, a course of gastric lavage preceding the operation. In this condition “alkalotic tetany” may be observed and call for treatment (p. 417).

**Hour-glass Stomach.**—This complication occurs as a result of scarring and contraction of a peptic ulcer on the lesser curvature of the stomach. The symptoms are often anomalous and the diagnosis is generally made by X-rays. There must be few physicians interested in gastric disease who have not confidently diagnosed an organic stenosis when at operation none has been found, the hour-glass contraction being entirely due to spasm. Thus a diagnosis of organic hour-glass stomach should not be made too hastily, but the patient should first be treated carefully as for an ordinary gastric ulcer. When true organic stenosis exists, surgery offers the only relief.

**Alkalosis following Alkali Treatment.**—This complication has already been briefly referred to, and up to the present too few physicians in general practice are aware of its dangers. As a rule it occurs only when alkalis have been taken in great excess, but in some patients it has followed relatively small amounts. The occurrence of frequent vomiting and the coexistence of organic renal disease are especially liable to induce alkalosis. The cardinal symptoms are listlessness, headache, nausea, vomiting and drowsiness, and in severe cases the condition may closely simulate uræmia. This similarity is enhanced by the fact that albumin may be found in the alkaline urine, and the blood

urea is always high—even up to 300 mg. per cent. The chloride content of the blood is greatly lowered. The treatment consists in the stoppage of alkalis, and the free administration of normal sodium chloride solution by mouth, rectum, or even intravenously when coma threatens. Ammonium chloride in doses of 15 gr. (0.9 gm.) given by the mouth in capsules three or four times daily is also of value.

#### MEDICAL ASPECTS OF SURGERY IN RELATION TO PEPTIC ULCER

Apart from perforation, a number of problems affect the physician in relation to the surgical treatment of peptic ulcer and its complications. Some of these, such as organic pyloric stenosis and hour-glass stomach, have already been discussed.

The physician is fairly often faced with the fact that treatment of a case of peptic ulcer has failed or recurrence has taken place. Failure may be due to a number of causes affecting the patient, his temperament, his non-adherence to rules of treatment, his occupation, his domestic circumstances and other matters outside the doctor's control. Moreover, failure may be due to unsuspected complications. Surgery is then frequently advised, and the commonest operation at present is gastro-enterostomy. On the other hand, partial gastrectomy in suitable cases and under favourable conditions is being more and more frequently carried out.

The decision to advise operation is sometimes difficult, but the following points are among those which should influence the physician in recommending surgery:—

1. The age of the patient—the older the patient the greater the surgical risk.
2. The duration of the history of ulcer—the possibility of operating on an acute ulcer must always be excluded.
3. The presence of organic pyloric stenosis with very persistent delay in emptying the stomach. The difficulties of excluding œdema and pylorospasm have been indicated.
4. Failure to obtain cure after fully adequate and prolonged medical treatment. Many failures and recurrences are undoubtedly due to inadequacy of treatment.
5. Failure (willing or unwilling) on the part of the patient to carry out medical treatment, especially when the patient is the bread-winner.
6. Risk of the onset of early carcinoma in prepyloric gastric ulcer.

The choice between gastro-enterostomy and partial gastrectomy raises certain points for consideration, some of which are beyond the scope of this work. The following matters are, however, of general importance:—

1. The immediate surgical risk.
2. The possibility of complications and sequelæ.
3. The possibility of failure to afford relief.

There is no doubt whatever that the operative mortality from partial gastrectomy is much higher than from posterior gastro-enterostomy. Against this may be set the fact that since hyperchlorhydria is common in peptic ulcer, a partial gastrectomy, whereby part at least of the acid-producing portion of the stomach is excised, may reduce the acidity, whereas gastro-enterostomy is not so successful in this respect. The chief danger of persisting hyperchlorhydria after the simple short-circuiting operation is jejunal ulceration at the stoma, referred to below. A sequel to be remem-

bered after a successful partial gastrectomy is the occasional development of anæmia. Partial gastrectomy is obviously the correct operation if any suspicion of carcinoma arises.

It is impossible to discuss here the opinions of different surgeons, but it may be said fairly that in most cases the first preference is for simple gastro-enterostomy with its minimal surgical mortality, partial gastrectomy being reserved for special cases, such as young persons with no stenosis and with marked hyperchlorhydria, and for those in which jejunal ulcer has followed the simpler operation.

**Jejunal or Gastro-jejunal Ulceration.**—This sequel to gastro-enterostomy, especially for duodenal ulcer, is unfortunately fairly common, occurring generally within a year or two, or even less, after the operation. It is believed to depend on persistence of the same set of circumstances in the stomach as before operation, and especially hyperchlorhydria. The new ulcer, situated at the stoma, in no way differs from the ordinary peptic ulcer of the stomach or duodenum, and must be treated on identical and rigid medical lines. If strict treatment fails, the jejunal ulcer may be excised, the stoma closed and a partial gastrectomy carried out. The operative mortality for this operation is naturally high, but it may require to be faced at a suitable time after the occurrence of the most frequent complication of jejunal ulcer, namely, hæmatemesis and melæna. Partial gastrectomy is easier in these circumstances when the original peptic ulcer is in the duodenum or near the pylorus. The operative difficulties are much greater when a deep penetrating ulcer of the lesser curvature is the primary lesion.

**Special Medical Treatment before and after Operation.**—Whichever operation is carried out, much can be done to ensure a successful result by careful pre-operative treatment. The stomach is often atonic, or emptying greatly delayed, and persistent vomiting with dehydration may have occurred. Except after recent hæmorrhage, the stomach may be gently washed out with warm water, and food for a few days prior to operation should be given in concentrated form (eggs, junket, jellies) with a minimum of residue. Fluids, such as glucose saline, should be supplied intravenously. By such measures the risk of dehydration and post-operative dilatation of the stomach is reduced, the organ to some extent recovering its tone.

Following operation, precautions are again essential to re-educate the stomach to an entirely new set of anatomical and physiological circumstances. This is particularly necessary after gastro-enterostomy, since a quite unaccustomed bulk of food is rapidly discharged from the stomach into the jejunum through the stoma. In practice it is best to start with a strict ulcer diet and to develop this in amount and variety very slowly. Although many patients after gastro-enterostomy seem to be able to eat "anything and everything" it is most injudicious to allow them to do so.

**Failure after Gastro-enterostomy.**—Failure after partial gastrectomy raises no discussion, since nothing further can be done. Failure to cure the peptic ulcer after gastro-enterostomy, or even to relieve symptoms, is unfortunately not infrequent (quite apart from the sequel of jejunal ulcer), and requires consideration. Pylorospasm and flatulence are common and their treatment has already been discussed. Periodic bilious regurgitation from the duodenum, resulting in vomiting, nausea and inability to eat, is sometimes met with when the pyloric sphincter does not function, or functions abnormally. The exact mechanism in these cases is not fully understood and the results

are particularly distressing, since medical treatment is of little value. In such patients the question of "undoing" the gastro-enterostomy and closing the stoma will arise, and this treatment may be successful in spite of the risks of adhesions.

#### A DIET FOR PEPTIC ULCER

##### *On Waking—*

Glass of milk.

##### *Breakfast (9 a.m.)—*

Orange juice or tomato juice, 1 oz. well diluted with water, or 50 mg. ascorbic acid.

Strained porridge with milk.

1 egg, boiled, scrambled or poached, or grilled or steamed white fish.

2 thin slices of toast, buttered cold.

Weak tea.

Honey or jelly.

##### *11 a.m.—*

Glass of milk, or Benger's Food.

Plain biscuit.

##### *Lunch (1 p.m.)—*

White fish (cream or soufflé); or minced rabbit, chicken or tender meat; or tripe, well steamed and minced.

Potato, mashed or purée.

Carefully sieved green vegetables, or carrot or turnip.

Fruit jelly or purée of fruit; or junket or egg custard or milk pudding.

Serve with cream or milk.

##### *3 p.m.—*

Glass of milk.

Plain biscuit.

##### *Tea (5 p.m.)—*

Weak tea, freshly infused.

2 thin slices of crisp toast, buttered cold; honey, syrup, treacle, or jelly.

Plain biscuit or sponge cake.

##### *Dinner (7 p.m.)—*See Lunch.

##### *Supper (9 p.m.)—*

Glass of milk, add Ovaltine, Horlick's, or Benger's if wished.

Plain biscuit.

##### *During Night—*

A glass of milk should be kept at the bedside to be taken if awake during the night.

#### *General Directions*

Try to take 2 pints of milk daily and use butter and margarine freely. A small teaspoonful of Marmite should be taken daily either in milk or hot water or spread on bread. Fried food in all forms is forbidden. Avoid twice-cooked meat, highly seasoned foods, spices, pepper, curries, vinegar, relishes, pickles, chutney and mustard.

Take your meals regularly and without hurry. Chew thoroughly. Large meals are harmful. It will be an advantage if you can rest for fifteen to thirty minutes after the principal meals.

**DIETETIC TREATMENT OF GASTRO-DUODENAL HÆMORRHAGE**  
(MODIFIED FROM MEULENGRACHT)

Arranged for Two-hourly Feeding

(Witts, *Brit. Med. Jour.* (1937), i. 851)

Feeds by Day.	Food.	Day.		
		1.	2.	3 and sub- sequent.
1	Whole milk (fresh or dried) . oz.	5	5	5
	Patent barley or strained porridge .	Portion	Portion	Portion
2	1 egg beaten up in milk . oz.	5	5	5
	Buttered rusks or cream crackers .	..	1	2
3	Whole milk (fresh or dried) . oz.	5	5	5
	Marmite to taste . . . .	..	..	..
	Barley sugar . . . . oz.	1	1	1
	Thin crustless white bread and butter slices . . . .	..	1	2
4	Strained orange or tomato juice . oz.	1	1	1
	Vegetable purée . . . .	Portion	Portion	Portion
	Pudding . . . . .	"	"	"
	Cream . . . . . oz.	1	1	1
	Boiled or steamed fish . . . .	..	..	Portion
5	1 egg beaten up in milk . oz.	5	5	5
	Barley sugar . . . . oz.	1	1	1
	Buttered rusks or cream crackers .	..	1	2
6	Whole milk (fresh or dried) . oz.	5	5	5
	Fruit purée . . . . .	Portion	Portion	Portion
	Pudding . . . . .	"	"	"
	Cream . . . . . oz.	..	1	1
	Thin crustless white bread and butter slices . . . .	..	1	2
7	1 egg beaten up in milk . oz.	5	5	5
	Black treacle or barley sugar . oz.	1	1	1
	Buttered rusks or cream crackers .	..	1	2
8	Whole milk (fresh or dried) . oz.	5	5	5
	Fruit purée . . . . .	Portion	Portion	Portion
	Pudding . . . . .	"	"	"
Feeds at Night (when awake)	1. Whole milk (fresh or dried) . oz.	5	5	5
	2. 1 egg beaten up in milk . oz.	5	5	5
Between Feeds	Strained orange or tomato juice . oz.	1	1	1
Approximate caloric value . . . .		2,545	3,118	3,624

### CANCER OF THE STOMACH

The majority of cases of cancer of the stomach are at present unfortunately not recognized until radical operation is impossible and the physician is only concerned with palliative treatment. Our aim must therefore be, even in the present very uncertain state of our knowledge, to attempt to prevent the occurrence of cancer of the stomach or to recognize its onset at the earliest possible stage.

It is suspected by many that chronic organic gastritis is a frequent precursor of carcinoma, and gastritis should receive adequate treatment.

It is known that cancer of the stomach may be superimposed on chronic peptic ulcer, and especially on the so-called prepyloric ulcer. A chronic peptic ulcer in this situation should thus receive very special care to ensure permanent cure.

The early diagnosis of cancer of the stomach is not within the scope of this book, but unexplained sudden dyspepsia in people over forty should always be regarded with suspicion and radiological investigation at once undertaken. In cases of cancer of the stomach recognized sufficiently early partial gastrectomy does offer a chance—the only chance—of permanent cure, but so far three-quarters of the “operable” cases die within five years. Deep X-ray and radium treatment have been so far unsuccessful. If pyloric stenosis, due to the tumour, is extreme, a palliative gastro-enterostomy may be done, but the operative mortality in such cases is high and life is seldom much prolonged. Operation should never be attempted if the liver is found to be involved.

The physician is mostly concerned with palliative treatment, mainly directed towards the relief of gastric discomfort and to procuring adequate sleep. Death usually occurs within six to twelve months after the diagnosis has been made.

Carcinoma may affect the cardiac end or the body of the stomach, but the commonest site is near the pylorus, and signs of pyloric obstruction quickly appear. The stomach behind the growth becomes dilated and atonic and hydrochloric acid is absent from the gastric juice. Fermentation of food, delayed greatly in its passage through the pylorus, is inevitable, and pus and debris derived from an ulcerating growth add to the patient's discomfort. Lavage of the stomach (see p. 555) is therefore frequently required, sometimes several times a day, weak bicarbonate of soda solution (a teaspoonful to 1 pint of warm water) being commonly employed. We wish to urge emphatically the importance of this palliative measure, which is far too seldom employed. The diet, when pyloric obstruction is obvious, should be liquid or semi-solid only, but within limits it is often best to let the patient choose what he desires. Odd fancies may emerge, and ice-cream was the only food tolerated and desired by a patient of one of the writers.

Sleep may be obtained in the early stages by mild hypnotics such as carbromal, 10 to 15 gr. (0.6 to 0.9 gm.) at night, but sooner or later opium will be required both for sleep and to alleviate pain and discomfort. Tincture of opium or nepenthe, 20 to 30 minims (1.2 to 1.8 c.c.) of either, three times daily, may be given by the mouth, and finally the subcutaneous injection of morphine will be necessary. The usual dose of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 32 mg.) daily may suffice at first, but tolerance soon develops and the injections



should be given as often as may be necessary to afford mental tranquillity and relief of pain.

Anæmia always develops in carcinoma of the stomach and may show temporary improvement under treatment with liver extracts and iron.

Various complications, such as jaundice from secondary deposits in the liver, pleural effusion and femoral thrombosis, may all entail alteration or additions in treatment.

One rare variety of cancer of the stomach—leather-bottle stomach—presents many points of difference from the ordinary type. It is very slow in growth—there are proved cases of ten to fifteen years' duration—and pyloric obstruction does not ensue. The stomach, in fact, comes to resemble a long narrow inelastic tube, through which the contents can be seen to hurry during examination by X-rays. Emaciation becomes extreme, being only equalled in carcinoma of the œsophagus, and feeding is unsatisfactory. Milk, eggs, junket and fruit juices are generally acceptable, and alcohol (as spirits or sweet wines) may also be taken. Pain is often considerable in the later stages and opium is generally required. In this very chronic type of carcinoma it may eventually be necessary to administer quantities of opium far in excess of the usual fatal dose.

### ANOREXIA NERVOSA

#### *(Hysterical Anorexia)*

This serious functional disorder, which may be difficult to distinguish from pituitary cachexia (see p. 444), is much commoner in females than in males and occurs especially in adolescence and early adult life. The psychological causes are many, but whatever the origin of the condition the clinical progress is the same. The patient declines to eat, and after a time all desire for food is lost. Emaciation rapidly ensues, and unless treatment is successful death may result simply from starvation. The prognosis depends entirely on the possibility of alleviating the psychological origin of the disorder.

In by far the majority of patients removal from home surroundings is essential and the treatment is psychological. The closest co-operation between the physician and a carefully chosen nurse is required. Every attempt must be made by persuasion to feed the patient frequently, a mouthful at a time, and even when improvement begins the nurse must never leave the sickroom when food is before the patient.

### SOME COMMON DISORDERS OF DIGESTION

**Flatulence.**—This is accurately defined as “the state of having the alimentary canal charged with gas,” but is not to be regarded as abnormal except when in excess. In the stomach there is almost always the air bubble at the cardiac end, well shown in an X-ray film after a barium meal. In the intestines there is invariably a considerable volume of gas of mixed composition derived from the food during digestion, and although much of it is absorbed through the intestinal wall, some usually passes on to be expelled from the rectum.

Flatulence in excess is, however, generally referred to by doctors simply as flatulence, and is divided into two varieties—gastric and intestinal—both of which may be present together.

Gastric flatulence may be manifested simply by a sensation of fulness, by actual eructations of "wind" or by acute pain so severe as to simulate coronary thrombosis. It may be of organic or functional origin. In its simplest form it occurs in any acute gastric upset, and is relieved by vomiting—spontaneous or induced—or by a carminative such as peppermint. It is a frequent complaint in peptic ulcer of all varieties and in carcinoma; and particularly prominent and persistent in association with organic disease of the gall-bladder, especially gall-stones (p. 596). Its treatment in all of these conditions is dealt with elsewhere.

Functional gastric flatulence is painless and almost invariably caused by aerophagy or air swallowing, a habit easily established but difficult to eradicate. In some patients a simple explanation of the facts is sufficient for cure, but many resent and strongly deny the accusation that they are "air swallows." To convince them and start the purely psychological cure, a piece of cork held between the molar teeth or a length of tape tied quite lightly round the neck just above the larynx will act as deterrents to aerophagy. Local inflammatory conditions in the mouth or even a badly fitting denture may be accessory factors in establishing the habit, and should be remedied.

Intestinal flatulence of great severity may occur in the "paralytic ileus" which occasionally follows abdominal operations and in the "tympanites" of peritonitis or typhoid fever, but the treatment of none of these is discussed here. A common cause is an upset of intestinal digestion, especially of starchy foods such as new bread or potatoes, when a great excess of gas may collect to produce flatulence and colic. Curtailment of starch is the obvious remedy (see p. 560) but the acute distension and painful colic require immediate relief. Diarrhoea, if it occurs, generally gives ease with free passage of gas, and a turpentine enema (p. 565) by irritating the bowel may have the same effect. The passage of a soft rubber tube into the colon is of little avail if the excess of gas is in the small intestine. Local applications to the abdomen, much used in the past, such as hot bottles, poultices, counter-irritants and stupes, have been shown in recent experiments to be ineffective except in minor cases. Activated charcoal as an adsorbent (1 to 4 teaspoonfuls three times daily by mouth) has a limited effect in chronic intestinal flatulence. Provided the bowel is not organically diseased, Pituitary Extract or preferably Pitressin (Parke, Davis & Co.) is the one certain and rapid remedy, even although its side-effects may be unpleasant. Pituitary Extract contains 20 units in 1 c.c., whereas Pitressin (from which the Pitocin has been removed) is put up in phials of 10 units in 0.5 c.c. The dose given should be 10 units of either preparation.

**Water-brash.**—Water-brash consists in the outpouring of dilute saliva which suddenly fills the mouth. Its exact mechanism is unknown, but it may occur at intervals in almost every form of organic gastric disease. No treatment is possible except for the associated disease.

**Hiccup.**—This very troublesome symptom is due to sudden spasm of the diaphragm, and again is of very varying significance and importance. It may occur from quickly overfilling the stomach with food or drink, and is then arrested by holding the breath or by inducing sneezing. On the other hand, persistent hiccup, which exhausts the patient, is a sign of many important organic diseases of the bowel and elsewhere and may be troublesome after operations in the upper abdomen. It occurs in encephalitis

lethargica, intestinal obstruction, uræmia, hepatic cirrhosis, carcinoma of the stomach, to name only a few examples. The treatment of persistent hiccup is discussed in the section on Cirrhosis of the Liver (p. 589).

**Heartburn.**—This term is used to describe a peculiar burning sensation presumed to be in the œsophagus, but its exact situation and ætiology are very obscure. It was formerly thought to be due to regurgitation of acid from the stomach into the œsophagus, but it is now known that it may occur even when achlorhydria is present. A drink of sodium bicarbonate as a rule affords relief.

**Nausea.**—This symptom, which it is difficult to describe better than “a feeling of sickness unaccompanied by actual vomiting,” is also met with in a number of bodily disturbances, quite apart from gastro-intestinal disease. It is complained of frequently in the early months of pregnancy, in migraine, in ocular astigmatism, in fainting, and in diseases of the stomach and gall-bladder. It may be one of the very earliest symptoms of carcinoma of the stomach and is a constant feature of alcoholic gastritis. The treatment required is concerned with the cause and no individual therapeutic description is possible.

### SOME UNCOMMON DISEASES OF THE STOMACH AND DUODENUM

**Syphilis** is rare and affects the stomach as a gummatous infiltration resulting in deformity or a mass large enough at times to be mistaken for carcinoma. The resemblance to carcinoma is enhanced since hydrochloric acid is absent or greatly diminished.

If syphilis is suspected, either from the history or from the evidence of a positive Wassermann reaction, a rapid trial of antisyphilitic treatment (p. 210) should be carried out. There appears to be a consensus of opinion in countries in which gastric syphilis is more common that potassium iodide in full doses is superior to the arsenical remedies. It must always be remembered that a positive Wassermann reaction does not exclude in any way a diagnosis of carcinoma.

**Acute dilatation** due to sudden atony is met with occasionally after upper abdominal operations and rarely during the course of acute specific fevers and pneumonia. The characteristic symptom is persistent vomiting of large quantities of dark but not fæcal fluid (“black vomiting”), which may pour out of the mouth unaccompanied by retching. Collapse and dehydration are extreme and treatment is always urgent. A narrow stomach tube, as used for the fractional test meal, is passed at once, and the stomach kept empty by repeated aspiration. Shock and dehydration are dealt with by the methods described elsewhere. Unless symptoms cease within forty-eight hours, jejunostomy should be carried out, if necessary under local anæsthesia, and the patient fed by this route until the stomach has recovered its tone.

**Chronic Duodenal Ileus (or Stasis).**—This uncommon condition is believed to be due to visceroptosis, to some congenital malformation or to an anatomical variation in the position of the mesenteric arteries which cross the duodenum. Diagnosis is difficult without confirmation by X-rays, and the symptoms are anomalous. Persistent headache, vomiting and pain simulating duodenal ulcer or cholecystitis are among the most common complaints.

Visceroptosis should be treated as described elsewhere (p. 566), and rest

after meals in a position found by experience to give relief should always be advised. In some patients administration of a pint of normal saline on an empty stomach flushes out the duodenum and arrests the symptoms. In severe cases surgical measures such as colopexy and duodeno-jejunostomy have been carried out, but surgery in this condition must still be regarded as in an experimental stage.

### GASTRIC LAVAGE AND SPECIAL METHODS OF FEEDING

**Gastric Lavage.**—In an adult gastric lavage may be required for the treatment of a variety of conditions, such as narcotic poisoning, chronic gastritis and pyloric obstruction.

Senoran's aspirator is a useful apparatus for the purpose but few practitioners possess the complete instrument, the rubber parts of which quickly perish. The ordinary stomach tube is all that is required, attached to a funnel by a glass connection and a short length of rubber tubing. A graduated cylindrical funnel is convenient, but if a filter funnel alone is available the fluid must be measured in the container from which it is poured. The stomach tube generally used is No. 18, Standard English Catheter Gauge, but some prefer a No. 24. The French (Charrière) gauge is no longer employed, and, in ordering, the description "Jacques" is unnecessary. The stomach tube, unlike the fine Ryle tube used for fractional test meals, is not marked at 18 in. from the tip (the average distance between the incisor teeth and the stomach), but it is advisable to make this mark with a narrow ring of adhesive tape or with thread tied fairly tightly round the tube. Except in emergencies, such as poisoning or when the patient is unconscious, careful instructions must be given so that the tube passes easily. There are two essentials—he must sit up and sit forward, with the chin well down on the chest, and he must breathe regularly and quietly all the time to avoid retching. The tube is wet after being sterilized by boiling and no further lubricant is required. The tube is passed slowly but deliberately until the mark (18 in.) is at the teeth; but in conditions in which the stomach is often dilated, e.g., chronic gastritis, an inch or two more may be necessary. It is generally best, especially when the stomach is dilated, to turn the patient on his side after the tube has been passed.

The fluid used for lavage is allowed to flow slowly into the stomach, using a very small head of pressure, the soft rubber connecting tube being first held and squeezed to expel air. Not more than one to one and a half pints of warm water should be introduced at one time. When the required amount has entered, the funnel (just before it is empty) is lowered and inverted over a basin and the stomach contents are removed by siphonage. The procedure is repeated until the return from the stomach is clear. The amount of fluid used and the amount returned is measured, and the difference between the two readings indicates the volume of the original gastric contents. After gastric lavage has been successfully accomplished on one or two occasions the patient learns to pass the tube on himself and the whole procedure loses its original unpleasantness.

**Nasal Feeding.**—This method is required more often in children than in adults. An ordinary soft rubber catheter, which is about 14 in. in length, of No. 4, 5 or 6 Standard English Catheter Gauge, according to age, is suitable for a child. In an adult No. 7 to No. 10 gauge is recommended, but a catheter

is really too short and reaches only a short distance down the adult œsophagus. Great care is therefore necessary, especially if the patient is unconscious or semi-conscious, for coughing may easily dislodge the tube, and aspiration into the bronchi occurs. For this reason, both in children and particularly in adults, the patient should be turned on one side after passing the tube, since, in case of accident, there is more chance of fluid being ejected by the mouth and less of insufflation. It is often advisable to start the feeding with sterile water for safety.

The catheter should be lubricated with boracic ointment and passed along the floor of the nose.

Whenever possible œsophageal feeding through the mouth should be preferred in an adult.

**Œsophageal Feeding.**—This method is used for the administration of food or glucose to unconscious patients and, rarely, for forced feeding. One of us uses a firm stomach tube of No. 10 Standard English Catheter Gauge, but in practice the ordinary stomach tube of No. 18 or 24 gauge attached to a funnel by the usual glass and rubber connection is quite satisfactory. The tube of smaller calibre has the advantage that it can be left *in situ* for a period without embarrassing the breathing.

## DISEASES OF THE INTESTINES

### INTRODUCTION

It would be convenient to consider treatment under the separate headings of small intestine and colon, but in practical medicine this is generally impossible. In many diseases both the small and large intestine are involved, although in different ways and in differing degrees. Few diseases capable at present of exact definition, interpretation and rational treatment affect the small intestine; many more affect the colon, and are described separately in textbooks.

**Chemical Functions.**—The small intestine is concerned, over its great length and surface-area, with the digestion and absorption of food, the main absorption taking place in the last part of the ileum. So far as treatment is concerned, the functions of the small intestine may be upset in two chief ways:—

1. There may be deficiency of absorption of normal essential substances—products of digestion of proteins, carbohydrates and fats, and the necessary vitamins and minerals. Defective absorption may at times be due to undue rapidity of passage through the ileum, thereby affecting the function of the large intestine.
2. There may be absorption of substances injurious to the body—poisons (organic and inorganic), bacterial toxins.

These two conditions obviously involve entirely different lines of rational treatment.

The normal functions of the colon are chiefly concerned with excretion. About 350 gm. of chyme, containing very small amounts of the products of digestion and 90 per cent. of water, normally pass through the ileocæcal valve in a day (Hurst). The average weight of fæces passed daily is 135 gm., containing 75 per cent. of water, and no sugar, coagulable protein or other

soluble substances. Thus absorption of much water and of the small amount of nutritive substances which enter the cæcum take place in the proximal colon. The distal colon and rectum merely act as reservoirs, until the important reflex act of defæcation occurs, and this obviously has important bearings on the question of so-called "rectal feeding" and "nutrient enemata."

**Intestinal Movements.**—The movements of the small intestine are chiefly of two kinds—active and frequent peristalsis, causing rapid movement and mixing of chyme, and slower segmentation. The upper part of the small intestine escapes the brunt of many diseases because of the rapidity of passage of its contents, but as the lower ileum is reached, where the main absorption of digestive products takes place, the passage is slower, and this part of the small gut is generally most seriously involved and injured. The rationale for increasing peristalsis and hurrying material through the bowel in certain diseases is thus plainly seen.

The normal movements of the colon are quite different and have been described as "mass movements." A single powerful peristaltic wave, occurring only at long intervals, pushes along a large mass of material.

The rectum is chiefly concerned with the finely adjusted reflex act of defæcation.

**Bacterial Flora.**—The bacterial flora of the intestine has bearings on treatment, quite apart from the problems created by the presence of invading and pathogenic micro-organisms. In the adult, streptococci predominate in the upper part of the small intestine, but in the ileum, with its slower movements, coliform organisms are chiefly found. These facts have been proved in samples taken during surgical operations. In the colon and rectum an enormous number and variety of micro-organisms abound, many of them saprophytic and harmless, but other normal inhabitants, such as streptococci, coliform bacilli, and gas-gangrene bacilli, may become pathogenic. The distribution of the bacterial flora in the whole length of the intestines may be greatly changed in disease, but also may be considerably influenced by treatment (see p. 560).

**Nervous Mechanism.**—The nervous control of the bowel, as it affects not only the ordinary intestinal movements but the reflex act of defæcation, is of the utmost importance in intestinal disease and its treatment. The control is a dual one, both local and central, and rational treatment may be required either to influence the bowel locally or to influence the whole patient through his central nervous system.

## DIARRHŒA

Diarrhœa consists essentially in the passage of loose or watery stools. A very rough distinction may be made between diarrhœa arising in the small intestine and that commencing only in the colon; in the former the motions tend to be watery, in the latter only loose and unformed. The stools in diarrhœa may contain excess of fat or starch, blood, pus, excess of mucus, abnormal pigments or deficiency of pigments. The necessity for careful examination, by naked eye, by the microscope and sometimes by chemical analysis, cannot be over-emphasized in order to ensure correct diagnosis and treatment.

Common general varieties of diarrhoea are:—

1. Infective and toxic.
2. Gastrogenous.
3. Nervous and lenteric.
4. So-called carbohydrate dyspepsia.
5. Pancreatic and fatty.
6. Endocrine, *e.g.*, in Graves' disease.

**Infective and Toxic Diarrhoea.**—The toxic and infective group is by far the largest and correct diagnosis is very essential for treatment. The whole range cannot be covered here, but this group includes food poisoning, dysentery, typhoid fever, organic and inorganic poisons, ulcerative colitis, and the toxic diarrhoea of nephritis. Special and specific methods of treatment are found elsewhere, but general principles applicable to most cases (excluding infants and children, p. 296) may be considered in detail.

These general principles are:—

*Rest in Bed and Warmth.*—This is essential when the diarrhoea is severe and especially if fever is present. Warmth to the abdomen is best applied in these cases by rubber hot-water bottles easily laid aside when the bowels are moved. Poultices and hot wet applications are nowadays no longer required. When fever is absent, and especially in collapse, hot bottles to the feet may also be desirable.

*Starvation, but Adequate Supply of Fluid.*—In this important aspect of treatment much turns on whether the stomach is also involved in the infective or toxic condition; if it is, food of every kind should be strictly withheld in the early stages. Fluids must be given by other routes to combat the rapid dehydration, which may be serious in an adult but still more serious in infancy and childhood. If the effects of a known poison are recognized, or a clear history is obtained, the appropriate antidote is administered and the stomach should be washed out. If the stomach is not seriously involved and vomiting is absent, plain water should be given at frequent intervals by the mouth. Both very hot and very cold drinks are well recognized to increase the symptoms and should be avoided. When vomiting is present, the fluid must be introduced by intravenous or slow subcutaneous injection (for Technique, see p. 925). For intravenous use a sterile solution of 0.85 per cent. (*i.e.*, normal) sodium chloride with 6 per cent. glucose added is employed; for slow "drip" injection normal salt solution alone is required. Occasionally, as in bacillary dysentery, it may be valuable treatment to introduce, directly into the stomach, through a fine tube (as used for fractional test meals), a pint of warm normal saline. This is not absorbed, but passes rapidly through the whole length of the intestine, washing out debris and toxins in a watery diarrhoea. The special methods to replace fluids and make up for the great loss of chlorides which occur in cholera are described elsewhere (p. 252).

*Diet.*—When an exact diagnosis has been made, the problem of feeding the patient at once arises, and the arrangements to be made must differ greatly in, for instance, long diseases such as enteric fever and short illnesses such as the simpler forms of food poisoning. In the latter, when after two or three days the acute symptoms are passing off, the complete rule of starvation must be relaxed and feeding commenced slowly. Barley water

is often used as the first change from water, but the actual feeding is best begun with arrowroot made up with water only, not with milk. Whey may also be acceptable at this stage or gelatin preparations such as Brand's essence. Later, milk and junket and sweetened fruit juices are commenced, and gradually as the patient improves the full diet is restored.

*Drugs.*—These may be required for five main purposes:—

- (a) To provide an antidote to a known poison.
- (b) To exaggerate an acute diarrhœa and quickly rid the bowel of an irritant. This method is particularly suitable in the ordinary simple forms of gastro-enteritis, and castor oil ( $\frac{1}{2}$  to 1 oz.) is the most valuable drug and has stood the test of time. It acts by increasing the peristalsis of the whole gastro-intestinal tract.

Calomel in small doses of  $\frac{1}{12}$  to  $\frac{1}{8}$  gr. (5 to 8 mg.) given at two-hourly intervals has also many advocates, but is much less used than formerly.

- (c) To arrest, or partially to arrest, severe and continuing diarrhœa which is weakening the patient by exhaustion, dehydration, pain or sleeplessness.

Opium and its alkaloids and kaolin are the two important remedies required; bismuth preparations, tincture of catechu and chalk are useful adjuvants and astringents.  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. (11 to 16 mg.) morphine or  $\frac{1}{4}$  gr. (16 mg.) codeine may be injected in adults, and a very well-known mixture for oral administration in adults is as follows:—

R $\bar{y}$  Tinct. Opii. . . . . ℥v to ℥x (0.3 to 0.6 c.c.)  
 Tinct. Catech. . . . . fl. dr. i (3.6 c.c.)  
 Mist. Cret. . . . . to fl. oz. i (28.4 c.c.)  
 Dose.—fl. oz. i (28.4 c.c.) two-hourly, or as required.

Kaolin, a china clay, which is a most efficient adsorbent, is particularly useful in chronic diarrhœa, and is often combined with charcoal if abdominal flatulence and distension are present. Kaolin is not absorbed from the bowel, and large doses may be given simply mixed with water. An average dose is  $\frac{1}{2}$  to 1 oz.

Gripping and tenesmus, which exhaust the patient, are best relieved by opium or belladonna and by the application of heat to the abdomen. Suppositories should seldom be employed, but a starch enema (the opium often added is useless) may give relief.

The treatment of acute intestinal flatulence and distension has already been discussed (p. 552).

- (d) To treat circulatory collapse. This occurs only in the severest forms of continued diarrhœa, and apart from warmth and large quantities of fluid, which are essential, any of the following drugs may on occasion be required:—

Alcohol (in certain cases only).  
 Methedrine (0.75 to 1.5 c.c. intravenously).  
 Nikethamide (2 c.c. by intravenous injection).



- (e) To change the bacterial flora of the bowel. This method has a very limited application, but in some forms of chronic diarrhoea it may be useful to administer *Bacillus acidophilus*. Spriggs recommends that 4 oz. of a pure culture of *B. acidophilus* should be given daily in a single dose in milk, and care must be taken that the culture is obtained from a reliable source which will guarantee that the organisms are alive. In most samples a minimal bacterial count of 250 million per c.c. is guaranteed and the directions state the period after preparation within which the culture must be used. Lactose should be taken freely with every meal to provide abundant pabulum for the bacillus—controlled experiments have clearly shown that this is an essential part of the treatment.

**Gastrogenous Diarrhoea.**—This special variety can only be suspected when no free hydrochloric acid is found to be present in the stomach after a test meal. The treatment consists in the administration of dilute hydrochloric acid in 1-drachm (3·6 c.c.) doses mixed with lemonade or orange juice to be drunk throughout the course of the meals.

**Nervous and Lienteric Diarrhoea.**—This is more a social trouble than an actual disease, but its occurrence can be devastating to an individual who must attend a public dinner and make a speech, or to a student sitting an important examination. Irritant foods and spices must be avoided beforehand and neither very hot nor ice-cold dishes should be taken. A sedative drug should be employed, and  $\frac{1}{2}$  to 1 gr. (0·03 to 0·06 gm.) phenobarbitone and 10 to 15 minims (0·6 to 0·9 c.c.) tincture of belladonna may be tried in turn or in combination to control the diarrhoea. Closely allied to this form of diarrhoea is the “hair-trigger colon” which often afflicts patients who have suffered from severe enteritis, such as dysentery, it may be several years previously. Such patients are particularly susceptible to chill, and whenever they are cold (*e.g.*, after a journey in an open motor car) diarrhoea which is quite uncontrollable may return for a few hours. They learn to avoid chill and should wear for a long period a “cholera belt” (the modern variety of silk and wool is best) around the abdomen.

**Intestinal Carbohydrate Dyspepsia.**—The diagnosis of this condition is often missed if the stools are not properly examined for starch granules. The essential clinical features are abdominal discomfort and great gaseous distension of the colon, due to fermentation of starch which has passed too rapidly through the small intestine and escaped its proper digestion there. The main point here again is accurate diagnosis and treatment is very effective. It consists, first, in avoiding or diminishing starchy foods for a time and using sugars as the main supply of carbohydrates. Taka-diastase (Parke, Davis & Co.), a powerful starch-splitting ferment, is of great value, and enables some starchy foods to be taken. It is available both as a powder or tablet in doses of  $2\frac{1}{2}$  to 5 gr. (0·15 to 0·3 gm.), or as a liquid in doses of 1 to 2 drachms (3·6 to 7·2 c.c.), taken during or immediately after each meal. Rarely, at the outset, it may be necessary to use an opium derivative, such as codeine gr.  $\frac{1}{2}$  (0·03 gm.) or papaveretum gr.  $\frac{1}{3}$  (0·02 gm.) to reduce the rapid passage of food through the small intestine. With the above treatment the small intestine can generally be retrained to deal with starch quite effectively.

**Pancreatic and Fatty Diarrhoea.**—See p. 257, Sprue.

**Diarrhoea in Graves' Disease.**—This may be a particularly troublesome symptom, and may occur either as an early symptom of the disease when the clinical features are not striking, or in the late stages even after an extensive radical operation.

The treatment may require to be long continued, so that opium should be kept for emergency use only. Other sedatives may be tried, but such diarrhoea usually yields only to the specific treatment of hyperthyroidism as described on p. 423.

**Diarrhoea of Uncertain Origin.**—A large number of cases of chronic diarrhoea sent to hospital because no accurate diagnosis can be made, and because simple treatment is unavailing, prove to be due to some form of partial intestinal obstruction and often to tumour growth in the colon. The diagnosis is generally made by X-ray examination. If, after complete examination, no signs of tumour are found, the doctor must think of such conditions as ulcerative colitis, uræmia, Addison's disease, tuberculosis of the intestine, amyloid disease, or even chronic arsenical poisoning.

### CONSTIPATION

Constipation may be defined as delay in the passage of fæces through the intestine, or delay in their evacuation. Before commencing to treat a case of constipation it is necessary to know that this condition truly exists, and that the patient has not simply "lost confidence in his bowels" (Hutchison). It is therefore generally wise at the outset to stop, for two days at least, all drugs which the patient has generally been taking and watch the result. It must be remembered also that incomplete evacuation of the bowel may constitute constipation just as much as no action at all.

It is essential to have some simple classification on which rational treatment is based. One broad classification may be made at once into organic and functional types. *Organic* constipation is less common but more serious, and depends frequently on some mechanical obstruction or partial obstruction of the lumen of the intestine. The obstruction may be within the bowel—tumour, stricture, foreign body or fæcal impaction—or due to pressure from without—tumour, adhesions, chronic peritonitis. The treatment required is often surgical. Severe intra-abdominal pain, paralysis of the bowel and painful lesions of the anus such as piles and fistula-in-ano, may produce the same clinical effects as mechanical obstruction. *Functional* constipation is exceedingly common, and forms one of the most important chapters in all medical treatment.

Hurst's classification of true or functional constipation is as follows:—

1. Colonic constipation—due to defective movements of the musculature of the colon. The movements may be deficient, or excessive (resulting in spasm—spastic colon).
2. Dyschezia—due to imperfect action of the reflex act of defæcation.
3. Deficiency in bulk of the fæces—due to incorrect feeding, or to unusually complete digestion ("greedy bowel"). In this group the rectum is insufficiently distended to excite the reflex act of defæcation.

Since we may regard the more usual type of constipation which the physician is called on to treat as functional and not organic (this latter type

having first been carefully excluded), the following principles must be considered in relation to treatment.

**Psychological Factors.**—The influence of the mind on the ætiology of constipation (as on some of the problems of diarrhœa) is common knowledge. Some patients simply cannot move their bowels when nervous or worried, in unusual surroundings such as travel, or even at the commencement of a holiday. Workers on alternate day and night shifts are also at a disadvantage, and may be very worried at failure of a previously regular habit. Bodily fatigue is another factor of importance. In all these circumstances the nervous individual may develop great anxiety about his bowels, he begins to take purgatives without advice, and a bad habit is established.

The general line of treatment is obvious—reassurance that occasional failure of the bowels to act is of no consequence, and that purgatives are quite unnecessary. A sedative mixture alone may be sufficient, along with reassurance, to cure this form of constipation almost at once.

**Faulty Habits of Defæcation.**—This is certainly one of the worst types of constipation to treat, and is often contracted in childhood and at school. Civilization has brought about many changes in our habits, and defæcation after every meal, still common in savage races, is uncommon with us. Custom has gradually trained most people so that the reflex act of defæcation functions once a day, usually in the morning and most commonly after breakfast. This habit is the result of gradual training. In modern conditions the rush to school or to catch the morning train may greatly interfere with the habit, unless ample time is allowed; and the sensation of the “call to stool,” once voluntarily suppressed, may not easily return again throughout the day. Many schools and offices are very inadequately provided with the necessary conveniences, and there is much room for medical opinion to aid in remedying these matters. Once the habit of regular defæcation is completely broken, the patient becomes constipated and uncomfortable, and as a rule at once takes to cathartic drugs or to enemas and injections. These bad habits and errors in treatment may persist for life, unless training is established and drugs eliminated.

**Physical Exercise** assists regular bowel movements and improvements in this matter throughout the town-dwelling population have been enormous during the past twenty-five years. Apart from games and the ordinary types of physical activity, adapted as far as possible to the patient's desires and preferences, certain specialized forms of physical exercise are of particular value in constipated patients whose abdominal musculature is weak. These are known as “Swedish exercises,” and numerous small books on the methods employed are available. Riding, rowing, skipping and gardening are all valuable for selected patients. When active exercise is impossible, thorough abdominal massage may be essential.

**Diet.**—Constipation is very frequently the result of faulty diet. The diet may be too dry or too concentrated, and the remedy is to increase the fluid intake. A well-known simple remedy is the early morning drink of a glass of hot water, and, as Kantor points out, this remedy is of particular physiological interest. It is only at this time that the stomach and small intestine are empty, and the gastro-colic reflex is readily stimulated. The diet may be deficient, especially among the poorer citizens, in foods which add the necessary bulk to the fæces to excite the reflex act of defæcation, or slightly irritate the bowel and increase peristalsis. Examples of the first group are

vegetables such as lettuce, spinach, cabbage, cauliflower, onions, turnips, and "rough" cereals such as wholemeal and bran. The indigestible skins and seeds of fruits, many of which also contain mild cathartic organic acids, increase peristalsis. Examples are prunes, figs, apples, pears, etc.

An adequate amount of fat, especially butter, is of recognized value, being the normal stimulant for the outflow of bile into the intestine. Olive oil may be used as a medicine for the same purpose, either by itself or as mayonnaise with salads.

**Drugs.**—Constipation being usually a functional disease, drugs should play a very minor part in its rational treatment. Nevertheless it will be found in practical medicine that the physician must employ them in the earlier stages of treatment, and he must also use them for longer periods, even for life, in certain types of patient. For example:—

1. Patients who fail to respond to general advice, either from carelessness or lack of intelligence. Such patients always have to resort to drugs, and it is best that the physician should advise those which are most suitable.
2. Elderly patients, and chronic invalids suffering from paralysis, heart disease, etc.
3. Patients temporarily bedridden by illness, accident or surgical operations.
4. The residue of cases which for any reason fail to respond to rational treatment without drugs.

The general rules of drug treatment for constipation are:—

1. Avoid all severe purges and cathartics for regular or frequent use (castor oil is a valuable purge, but harmful for regular use).
2. Almost all drugs used for constipation tend to lose, after a time, their original efficiency—the patient's body becomes habituated to them.
3. Drugs used for constipation vary in the period required for their action—the dose must therefore be given at the correct time to ensure a morning evacuation.
4. A suitable dose must be found, which differs greatly in individuals, to give a single soft but not watery motion.

The number of drugs employed for constipation is endless; only those of proved value, with their special indications, need be mentioned.

*Alkaloids* which act on nerve endings in the bowel. The alkaloid most commonly used in gastro-intestinal disease is atropine (or belladonna). It is of great value in spastic colon (p. 570). Strychnine is a frequent constituent of pills and mixtures, but is probably of little value for increasing peristalsis in the dosage commonly employed.

*Vegetable Purgatives and Laxatives*, which act either by increasing peristalsis or as mild irritants to the bowel wall. Some of the chief members of this group belong to the anthracene series and include cascara sagrada, senna, aloes, rhubarb and phenolphthalein. All of these are useful for special purposes, and a most important point common to all is that they have less tendency to lose their efficiency after continuous use than other drugs employed for constipation. Senna and rhubarb are the most powerful, and unless the dose is carefully arranged may act in as short a time as four or

five hours. Rhubarb suffers from the disadvantage that constipation follows its use, and it is only suitable, but very valuable, as an occasional purge. Gregory's powder (which contains rhubarb, heavy and light magnesium carbonate and ginger) is well known for its efficiency both as an antacid and purgative after injudicious eating. Senna is best employed as senna pods, which are soaked overnight in cold water. In practice it is advisable to instruct the patient to prepare the next dose at the time the first is taken, and the correct number of pods to ensure one good bowel movement in the morning is quickly found by experience.

Aloes, or its active principle aloin, acts on the colon, and an average dose takes ten or twelve hours to act; it is a common constituent of many pills.

Phenolphthalein is not so much employed alone as formerly, but has the advantage of being almost tasteless.

The anthracene group are by far the most valuable and commonly employed drugs for the treatment of chronic constipation.

*Salines.*—These are not suitable for habitual use, in spite of wide advertising of their merits as laxatives in small doses; the hot water which dissolves them is really the useful remedy. The mode of action of the purgative doses of the salines has been in some dispute. The commonly accepted view is that they act by extracting water from the bowel wall or by preventing its absorption, but Hurst and others claim that they act on the neuromuscular mechanism of the bowel only after absorption. Sodium sulphate, magnesium sulphate and sodium phosphate are the best examples, and in suitable doses of  $\frac{1}{2}$  to 1 oz. (15.5 to 31 gm.) act very quickly, especially when dissolved in hot water, and should be taken before breakfast to ensure a loose and often watery motion soon after this meal. A disadvantage, even as an occasional purge, is that painful tenesmus may result, and if the whole dose is not evacuated at once, frequent small stools may persist throughout the morning. None of the saline purgatives is pleasant to take, and effervescent preparations such as *Pulvis Effervescens Co.* (B.P.) are often preferred by patients.

*Mercury Preparations.*—Calomel and grey powder are the only mercurial preparations commonly employed. Calomel decomposes in the intestine, liberating free metallic mercury, which is the active agent in increasing peristalsis of the small intestine. It is far less used nowadays than formerly, and is chiefly applicable as an occasional purge in "biliousness." The usual adult dose is  $\frac{1}{4}$  to 1 gr. (16 to 64 mg.) at night, followed by a saline purgative in the morning to remove the irritant metal.

*Inert Substances Increasing the Bulk of the Fæces.*—Careful and suitable dietetics is the best and most rational way of providing for an adequate bulk of fæces, but medicaments may also at times be usefully employed. Liquid paraffin, a mineral and non-absorbable oil, cannot be described as adding bulk, but it acts as a non-irritating lubricant and is often used in combination with other substances with good results. When liquid paraffin is given alone its great disadvantage is that it frequently leaks from the anus and soils the clothes; this, however, can often be avoided by its administration in a dose of one teaspoonful immediately after all meals, so that admixture with the food ensues. The best material to add bulk to the fæces is agar-agar, a dried preparation made from a seaweed, which is not absorbed but takes up a large amount of water. It may be given in shredded form, or as a powder—dose, 1 drachm (3.9 gm.) or much more, according to circumstances. Coreine (Brunet), described as a dried vegetable

mucilage, is also useful, the dosage being similar. A large number of emulsions of agar-agar and liquid paraffin are available, but it must clearly be remembered that most of them contain a purgative drug, on which their activity partly depends, and also that in many of these preparations the percentage of agar-agar is relatively small. Emulsio Paraff. Liq. Co. (B.P.C.) contains 50 per cent. of liquid paraffin, 0.75 per cent. agar and  $1\frac{1}{2}$  gr. (0.09 gm.) of phenolphthalein per fluid ounce. Dose, 1 to 4 fluid drachms (3.6 to 14.4 c.c.). Agarol (Warner), as sold in this country, is made up of 33 per cent. of liquid paraffin, 16 per cent. of agar jelly and 6 gr. (0.36 gm.) of phenolphthalein per fluid ounce. Agarol without phenolphthalein is not obtainable in Britain. Petrolagar (Petrolagar Co.) contains 66 per cent. of liquid paraffin and 20 per cent. of agar jelly. It can be obtained with or without  $1\frac{1}{2}$  gr. (0.09 gm.) of phenolphthalein per fluid ounce. Normacol (Norgine), marketed in Britain by Napp, is described as a desiccated plant mucilage with rhamnaceous glucosides, probably those of cascara. Treatment with these remedies may be valuable, but in many cases the continued use of phenolphthalein is contraindicated. Agar-agar should be prescribed alone, when the addition of bulk to the fæces is the sole object.

**Enemas and Colonic Irrigations.**—These have a limited field in the treatment of constipation, but have some important applications in special circumstances. The use of enemas for purposes other than the treatment of intestinal disorders, *e.g.*, very concentrated solutions of magnesium sulphate to reduce intracranial pressure, is outside of the scope of this chapter.

Enemas as used for intestinal diseases are described as high and low. High enemas (colonic lavage, colonic irrigation) are described separately; what follows refers to the usual low enemas, which are administered with a Higginson's syringe or, more commonly nowadays, with a soft rubber tube and funnel.

Low enemas act mechanically, as chemical irritants, as softeners of hard fæces, or by a combination of these effects. Thermal stimulation is unimportant and an enema introduced at higher temperature than body heat must be avoided. Those in common use are:—

**Soap and Water Enema.**—The amount commonly employed is 1 pint, and the soap acts as a mild irritant.

**Turpentine Enema.**—1 oz. of oil of turpentine is emulsified in 1 pint of ordinary starch solution. This is used particularly when there is excessive gas or flatus in the colon, and although its exact mode of action is really uncertain, its efficiency is undoubted.

**Olive Oil or Liquid Paraffin Enema.**—Five ounces or more, warmed to body temperature, are introduced slowly at night and are retained if possible until the following morning. A pad of cotton-wool should be placed between the buttocks, to avoid the results of leakage during the night. Olive oil and liquid paraffin, which both act equally well, are used to remove hard dry masses of fæces (scybala) from the rectum. Their power of softening must be slight and only superficial, and their lubricating effect is more important. With their help hard scybala can frequently be evacuated, and as the peristaltic effort of the bowel may be painful and spasmodic, a full dose of 10 to 20 minims (0.58 to 1.2 c.c.) of tincture of belladonna or an injection of  $\frac{1}{100}$  gr. (0.65 mg.) of atropine sulphate may be helpful. If this method fails, then evacuation of scybala by the gloved finger is required,

and a general anæsthetic may simplify the procedure. It is far safer to use the fingers than the handle of a spoon, as was formerly advised in textbooks, but at times a hard object may be essential to break up concretions.

The chief uses of enemas are in :—

1. Spastic constipation, see p. 570.
2. So-called dyschezia, when for any reason the reflex act of defæcation is lost or impaired.
3. In bedridden, old or paralysed patients.

On the whole enemas should be used sparingly, but they may have great temporary value in suitable cases.

*High Enemas* (colonic lavage, or irrigation) have a legitimate but restricted use in conditions in which it may be desired to apply some form of therapy directly to the mucosa, or simply to empty the colon.

A soft rubber tube is inserted not more than 2 or 3 in. into the rectum, and the fluid (warmed to body temperature) is allowed to flow in slowly. The pressure used should be the lowest possible to ensure success, and the reservoir should never be raised more than a foot or two above the bed.

For correct medical treatment a single tube only is required. The amount of fluid varies according to the underlying condition. In inflammatory or ulcerative lesions, when the therapeutic fluid is to be retained for as long as possible, *e.g.*, dysentery, ulcerative colitis, the amount will be less than 1 pint in acute cases, but more in chronic lesions (see p. 23, Chronic Dysentery). To empty the colon larger amounts of fluid—1 to 2 pints of plain warm water—may be used, injected very slowly. The fluid may reach the cæcum, as is shown radiologically after a barium enema. The gentle gradual distension of the colon excites peristalsis, and emptying ensues.

The second method, in which two tubes (a smaller for the injection and a larger for the evacuation) are employed, is useless; and the fluid seldom completely fills more than the rectum and sigmoid colon. Nevertheless this is the method frequently carried out in the fashionable cult of colonic irrigation, and gallons of fluid may be passed in by one tube and quickly out by the other.

We wish to state clearly our condemnation of frequent colonic irrigations so much advertised in the lay press of this country (and undertaken generally without medical advice) for the relief of intestinal toxæmia or stasis, and the many imaginary ills associated with this supposed ubiquitous complaint.

There is no doubt that frequent colonic irrigation greatly disturbs the whole normal physiological activity of the colon—nervous, muscular and secretory (mucous). Moreover, the individuals prone to resort to frequent “treatments” of this kind are generally of neuropathic type, and easily acquire the irrigation habit to their mental and physical detriment.

### VISCEROPTOSIS

Visceroptosis from the standpoint of treatment falls into two classes, depending on whether the dropping of the abdominal viscera is due to: (1) fall in intra-abdominal pressure, previously adequate; (2) bodily habitus.

In many persons, both male and female, the abdominal viscera may

occupy an unusually low position without any symptom whatever. Thus an X-ray diagnosis alone must always be guarded against, and a diagnosis of visceroptosis rests entirely on the presence of symptoms. The symptomatology in both classes is very complex, and a correct diagnosis may be far from easy. In consequence of this and because the means employed are very time-consuming, visceroptosis is on the whole badly treated, although the patients are often as useless and disabled for work as if they suffered from serious organic disease.

**Fall in Intra-abdominal Pressure, Previously Adequate.**—This group contains a very great preponderance of females, since its commonest cause is repeated pregnancy followed by inadequate attention to the restoration of abdominal muscle tonus after each confinement. The tendency to visceroptosis is increased when there has been rupture or stretching of the pelvic muscular floor, or unusual stretching of the abdominal wall. In both sexes, abdominal operations, especially if repeated, may bring about the same state of affairs. In this group, the mental factor, which is so prominent from the beginning in the second class, may slowly develop once the condition has become well established.

**Bodily Habitus.**—It would almost be correct to describe this group as due to "bodily and mental" habitus, by the time the patient reaches the consulting room. The patient starts with a certain type of bodily diathesis, consisting of a narrow chest, a long and narrow costal angle and a tendency to lordosis. This shape of body, and the abdominal symptoms of visceroptosis which may accompany it, are most commonly found in women, but are by no means infrequent in men. To this bodily habitus is added a general state of asthenia, with rapid mental and physical exhaustion. (It must be remembered that asthenia may occasionally be the chief symptom of serious organic disease, such as tuberculosis and gastric ulcer; it may also occur in patients who, because of an accident or otherwise, have been long confined to bed.)

In this type the mental factor is very predominant from the outset, and in addition to general symptoms the patient is constantly conscious of abdominal discomforts which are difficult to explain. In contrast to mucous colitis (p. 570) in which the physical disability is the outcome of a nervous state, here the mental condition must be regarded almost as a sequel to the bodily habitus. Hence it follows in this group that the first line of approach is to treat the physical state, while the mental outlook is strengthened to ensure the co-operation essential for cure.

The treatment necessary for the two groups of patients is different in a few respects, which are mentioned, but on the whole the remedies employed are the same for both.

In the first group the essential treatment is obviously prophylactic, and fortunately the after-care of pregnancy is now greatly improved. Massage and suitable exercises to restore the tonus of the abdominal muscles may be essential, both after pregnancy and at the correct interval of time after abdominal operations. The perineum must be repaired and any tendency to uterine prolapse prevented.

In the second group much could also be done, and perhaps in future will be done, by prophylactic physical training beginning at school. The good effects of physical training, even at a later age, has been plainly shown in recruits for the army found to be under-developed on enlistment.



It will no doubt continue to happen, however, that the physician is first faced with the problems of visceroptosis when both its physical and mental symptoms are well developed, and the general treatment is then as follows:—

**Improvement of Nutrition.**—Many of these patients are exceedingly thin, and in such cases before any other treatment is contemplated a serious attempt should be made to fatten them, both to improve their general condition and to increase their intra-abdominal supporting fat. This stage of treatment is much more easily carried out in an institution in which full dietetic facilities are available, but if the doctor takes trouble it can be done at home. At the beginning the patient is confined to bed, and a start is made with the best average diet that she will take. Almost invariably these patients have poor appetites, but extra nourishment is added between the ordinary meals which they must be persuaded to take “just like any other medicine.” They should be told that as their body improves in condition so they will need more food and their appetite will improve. The best extra food is milk, plain or flavoured with tea, coffee, chocolate or anything else that the patient fancies, or made up in the form of junket, custard, egg-flip or ice-cream. Ice-cream is often of great value in patients who say they “cannot take milk,” and many calories may be added in this way. In the rare cases in which there is actual sensitiveness to milk protein, glucose may be used but is not so effective. Butter should be given in as large amounts as possible, and many patients with poor appetites enjoy bread and butter if a little Marmite is added to the butter. Provided that the patient is helpful, it is seldom that weight is not gained while in bed, and after two or three weeks the patient may get up and slowly commence remedial exercises while still continuing the enhanced diet and, if possible, increasing it. Remedial exercises should be directed by an expert, in a class of several members to induce competition. A cold rub or cold shower bath, in patients who react, may be useful.

To obtain a permanent cure by these methods requires great perseverance and patience on the part of both patient and doctor, and when this is remembered it is not to be wondered that at present the failures outnumber the cures. These methods are only likely to be successful in patients who are moderately alert and below the age of forty; if they fail it is necessary to fall back on the palliative treatment of a mechanical support to the abdomen.

**Forms of Mechanical Support.**—Adhesive strapping is quite unsuitable, except as a temporary or trial expedient, and some form of belt or corset must be employed. These, if a good fit, increase intra-abdominal pressure and undoubtedly to some extent raise and support the abdominal contents.

Certain rules for the purchase and use of all belts and corsets in the treatment of visceroptosis, must be strictly adhered to:—

- (a) They must always be put on when the patient is lying down, never in the erect posture.
- (b) Perineal slings and straps are always uncomfortable and should if possible be avoided.
- (c) The belt or corset should never be taken from “stock,” but specially made or specially altered to fit the patient.

- (d) Some forms of belt or corset suit one patient whilst others do not. All good firms who supply them are therefore willing to lend samples of approximately correct measurement for a few weeks' trial; advantage of this should always be taken, and when the suitable pattern is found a copy should be made to measure.

In Britain, a number of excellent belts or corsets are available, and although only a few are mentioned, this does not exclude other excellent patterns. Of belts perhaps the best known are those of Curtis (London) and Salt (Birmingham). The Curtis belt consists essentially of a thin but strong metal plate, suitably padded, applied (when lying down) to the lower abdomen. It is held firmly in position by two strong but flexible metal arms, united over the vertebral column by a small padded saddle. The belt is comfortable to most patients, never unsightly in any circumstances, and the mobile arms allow the patient to sit down without difficulty. The only trouble encountered with some patients, especially when they are very thin, is that the pressure of the saddle over the prominent backbone may be intolerable. For this reason, as already stated, a belt of this kind should always be taken on trial. If unsuccessful, a similar metal plate enclosed in a corset may be tried (Curtis, Salt), or a corset alone in which side straps and buckles provide for support in an upward and backward direction. Corsets of this kind made by the "Camp" Corset Company are efficient in less severe cases and are readily obtainable. A point of some importance is that they closely resemble ordinary corsets, and the patient does not feel that she is wearing a surgical instrument. Directions for self-measurement are always supplied by the various makers, and whichever form of belt or corset is finally chosen, it must be given a reasonable trial of several months before any opinion about the result can be given.

**Constipation** is very common in patients suffering from visceroptosis, and must be treated (p. 561).

**Operations** of many kinds have been devised for visceroptosis, but all have signally failed and mercifully have all been abandoned. An abdominal operation of any kind is the last thing to be desired in these patients. There are, however, certain individual viscera which, if markedly displaced in the abdomen, may induce symptoms which can only be cured by operation. Chronic duodenal ileus may result from constriction by the mesentery and mesenteric vessels; the symptoms closely simulate those of duodenal ulcer. Extreme ptosis or dislocation of the spleen (so-called wandering spleen) may be followed by torsion of the pedicle or be associated with severe perisplenitis and pain. Removal of the spleen is then indicated. Lastly, severe renal colic (Dietl's crisis) may occasionally arise in nephroptosis. Dropping of the kidneys, if found incidentally during an abdominal examination, should never be mentioned to the patient, as it may simply exaggerate the mental aspects of the case.

### ENTERITIS

The general clinical term "enteritis," although it is not commonly used, except in the form "gastro-enteritis," is useful in that it covers all the organic inflammatory diseases of the intestinal tract.

Inflammation of the intestinal wall may be of many kinds, acute or chronic in its course, catarrhal, ulcerative or gangrenous in its pathology,

and due to many causes ranging from bacteria and their toxins, organic and inorganic poisons (mercury, lead, arsenic) and general metabolic disturbances such as uræmia. Most of these forms of enteritis are discussed elsewhere. The clamant general symptoms requiring treatment are diarrhœa (with its associated dehydration and collapse) and toxæmia due to absorption through the inflamed bowel wall. In many cases the exact cause of enteritis can be identified, and special treatment is indicated. In others (*e.g.*, chronic ulcerative colitis) the cause may be unknown or uncertain.

It is important to differentiate a true inflammatory enteritis from a functional disorder such as muco-membranous colic (formerly described as mucous colitis) in which the treatment is essentially different.

### CHRONIC REGIONAL ILEITIS

(*Crohn's disease. Chronic cicatrizing enteritis*)

This is an uncommon form of chronic enteritis, affecting the terminal part of the ileum and also spreading into the cæcum. It occurs chiefly in young adult males. The portion of bowel involved becomes thickened and rigid from inflammation, and this is followed by fibrosis, narrowing and ulceration. Tuberculosis has been suspected, because giant cells are often present, but these are probably "foreign body" giant cells associated with necrosis of tissue, and tubercle bacilli have not been found. The symptoms are those of partial intestinal obstruction, a sausage-shaped tumour may be felt, and on X-ray examination with barium a filling defect (the "string" sign) may be evident.

The treatment is essentially surgical. To minimize the operative risk a short circuit of the affected bowel is advised, followed by complete resection at a later stage.

### IRRITABLE COLON

(*Spastic colon*)

### MUCO-MEMBRANOUS COLIC

(*Mucous colitis*)

Under these headings may be included for convenience what really amounts to a whole group of intestinal disorders, somewhat similar in their ætiology and therefore in the principles of their treatment.

These conditions are not, in the earlier stages at least, to be regarded as a true inflammation or colitis, but as an entirely functional disturbance of the bowel wall and of its secretions. Nevertheless, if the adverse circumstances persist, any one of them may end in a true inflammation.

There are three main factors known to be concerned in the ætiology of this group, but there may be others.

1. Nervous and emotional instability.
2. The abuse of cathartics, enemas or colonic irrigations.
3. Disease elsewhere (in the gall-bladder, female pelvic organs, etc.) acting "reflexly" on the bowel. In any individual case only one or a combination of these ætiological factors may be important.

Spastic colon and muco-membranous colic are best regarded simply

as differing degrees of severity of the same disorder. The former is very common in both sexes; the latter is comparatively rarely seen nowadays in practice, and is chiefly encountered in women. In both there is tonic spasm of the colon wall, causing hardening and contraction, and the descending colon may be felt through the abdominal wall almost like a bar. Constipation is common, or alternating bouts of constipation and diarrhoea.

In "spastic colon," mucus is generally absent from the stools; in muco-membranous colic shreds of mucus or complete mucous casts of the bowel may be passed. Pain and colic are the chief subjective symptoms.

**The Nervous Aspect.**—After a thorough physical examination, made deliberately in part to impress the patient, assurance must first be given that the condition (as is often suspected) is not cancer. The remainder of the treatment consists essentially in rational psychotherapeutic treatment, and the symptomatic treatment of muscular spasm if this is present. The psychological aspects of every case will differ, and the scope of the examination and treatment cannot be discussed here. The spasm of the colon wall is best treated with 10 to 30 minims (0.58 to 1.7 c.c.) of tincture of belladonna thrice daily, or with  $\frac{1}{100}$  gr. (0.64 mg.) of atropine sulphate or 2 to 4 gr. (0.12 to 0.24 gm.) of papaverine. Morphine must never be used. Occupational therapy and a study of the whole mental and physical health of the patient are both important.

**Correction of Abuse of Purgatives.**—It will be found that many of these patients, especially those suffering from spastic colon, have treated their constipation by the frequent use of almost every purgative offered to the public. These must be forbidden, and permission only given for olive oil, liquid paraffin or agar-agar. The proprietary preparations which contain phenolphthalein (p. 565) should be avoided in these cases. Colonic lavage not only should never be advised but must often positively be forbidden, as sufferers from an irritable colon are only too prone to consider that it is "the very thing for them." A careful diet which, while avoiding coarse residue, maintains adequate bulk (see Appendix, p. 577), is a valuable aid to overcoming the purgative habit. Wholemeal breads, unsieved vegetables and fruits containing pips are avoided, but other fruits and vegetable purées should be taken freely.

**Reflex Spasm from Disease Elsewhere in the Abdomen.**—This is a difficult problem and calls for much care in diagnosis. It is only when disease in some other organ is proved up to the hilt that operation should be recommended in these patients. This is especially true in muco-membranous colic for two good reasons. First, the mental outlook of the patient as a rule makes any operation inadvisable on general grounds. Second, the pain in muco-membranous colic can be made, by the patient at least, to simulate almost any acute intra-abdominal disease. One of the writers has encountered a male sufferer from muco-membranous colic who in the course of years had five emergency abdominal operations performed in various hospitals. The man himself was convinced, and remains convinced by his colicky symptoms and passage of mucous casts, that there is "something alive" within his bowel, and that some surgeon will ultimately find and remove it.

Irritable or spastic colon is common and a condition for which rational treatment should always effect a cure. Muco-membranous colic, once the complete symptomatology has appeared, always presents a long and exceedingly unsatisfactory therapeutic problem.

### CHRONIC ULCERATIVE COLITIS

The treatment of this serious and fairly common disease centres in the first place round the problems of its ætiology. It must be stated that none of the hypotheses so far advanced has yielded anything approaching a uniform, satisfactory or specific line of treatment for the majority of cases.

Most physicians, therefore, continue to treat the disease on general lines, omitting all reference to ætiology. The general treatment will first be discussed and thereafter reference must be made to special methods of therapy for which good results have been claimed.

The disease is almost confined to adults, and it is curious that young children, who are so prone to intestinal diseases, should generally escape.

There is a gradually increasing body of clinical evidence that the disease may appear with great rapidity very soon after some acute mental or psychological disturbance, which suggests some nervous derangement of the mechanism of the bowel. But this view, although manifestly important, has not yet yielded any help in the treatment of the established disease, which even if it appears with great suddenness unfortunately shows little tendency to rapidity of cure. The fact that treatment is bound to be very prolonged, requiring the utmost patience both on the part of patient and physician, is the first thing to realize, once the diagnosis has been made and the common causes of diarrhoea associated with blood, mucus and pus in the stools have been excluded. The course of the average case is a series of ups and downs, and the main general features of the disease for which treatment may be required are fever, toxæmia, anæmia from hæmorrhage, loss of weight in severe cases and exhaustion and dehydration from the frequent stools. Pain is seldom, if ever, a serious matter in this disease, although abdominal discomfort is always present.

**General Treatment.**—*Rest in Bed.*—This is the first essential when the diagnosis has been made, and preparations must be made at once for a stay in bed of some months at least and, by no means uncommonly, for a year. A rough rule of value is that the patient must not be allowed up while there is fever, or when the stools number more than two or three in the twenty-four hours.

**Dietetics.**—This is important in this long-continued weakening disease, for many patients die simply from asthenia. Ulcerative colitis affects the colon alone, and not the small intestine in which all the processes of digestion and assimilation remain, for a time at least, quite unimpaired. The patient may be quite fat and plump at the commencement, and continue so for many months; rapid loss of weight is always a bad sign. A fully adequate diet of high caloric value should be given (see Appendix, p. 578) to mitigate the loss of blood in the stools and the general physical exhaustion. The diet should be free from coarse particles of cellulose, and spices or condiments must be omitted. In patients in whom the diarrhoea is extremely severe, temporary benefit may be obtained by a diet of pulped apple, although this cannot be continued for more than a few days because the caloric value is low. This diet, and a modification of it which has proved useful, is described on p. 580.

**Drugs.**—Some are required for the control of general symptoms, while others are used for their action on the ulcerated wall of the colon. Sleeplessness is common during the acute phases, when stools may be passed hourly

or even half-hourly. Subcutaneous injections of sedatives must be avoided and  $\frac{1}{4}$  gr. (16 mg.) of codeine by the mouth or  $\frac{1}{2}$  gr. (0.03 gm.) of phenobarbitone three times a day are generally effective.

Sulphaguanidine (p. 76) has recently been strongly recommended, but the results of its use are disappointing. Kaolin, kaolin-with-charcoal and other adsorbents have been much employed, but in the writers' experience have not been effective in controlling the diarrhoea. Charcoal is, however, of real use when there is colicky pain or gaseous distension. Tincture of belladonna, 10 to 30 minims (0.58 to 1.7 c.c.) in three equal doses daily, is of value when spasm of the colon is clearly recognized.

Anæmia is always present, and is treated with iron and ammonium citrate, 30 gr. (1.8 gm.) or more, three times daily. If the anæmia becomes severe, blood transfusion should always be carried out. Even when anæmia is mild in degree many physicians believe that small and repeated blood transfusions are the most valuable remedy we possess for combating the asthenia present in this disease.

**Local Treatment.**—Local treatment of the ulcerated mucous membrane of the colon presents difficult problems, and it is not easy to judge the effects of the various remedies fully. Local treatment should not be employed in the acute stages of the disease. The application of various drugs to the bowel wall by lavage can seldom be carried out successfully unless complete nursing facilities are available. Various drugs have been employed, and in every case it is of advantage not to persist with one of them too long but to change to another. A starch enema may be useful when there is much pain and tenesmus. Later, the bowel may be slowly washed out, every second day, with normal saline, flavine (1:200,000), mild silver protein (B.P.C.) ( $\frac{1}{2}$  per cent.), or tannic acid in strengths gradually increasing from  $\frac{1}{2}$  to 2 gr. (0.03 to 0.12 gm.) to 1 oz. of warm water. Whatever fluid is used, up to 1 pint should be allowed to run in very slowly under the lowest possible pressure, and the patient should be encouraged to retain the fluid for half an hour. It must be stated that all varieties of irrigation are now much less used than was our former custom.

In serious cases, when the measures outlined above have been unsuccessful, the question of surgical intervention to allow the colon to be washed out from above must arise. Two operations may be performed: (1) *Appendicostomy* or *cæcostomy*, allowing the insertion of a fine rubber tube to carry the irrigating fluid, and (2) *ileostomy*. The latter is the more serious operation in a very ill patient, but has the evident advantage of preventing the passage of faeces into the colon so that it can ultimately be thoroughly cleansed. Everyone with much experience must have seen some patients apparently recover as a direct result of one or other operation, but on the other hand almost an equal number die. It is probably the truth that the possibilities of these operations are as a rule only considered too late, when the risk of any surgical intervention is grave. But so far the results have not been sufficiently impressive to indicate early operation as the most hopeful treatment, either to save life or to shorten the disease.

**Specific Treatment.**—Certain forms of specific treatment, based on views concerning ætiology, must now be discussed.

**Antidysenteric Serum.**—This method has been recommended especially by Hurst, who believed that the majority of cases of ulcerative colitis are due to a dysentery bacillus, even although the organism cannot be isolated

from the stools. He advised, after preliminary desensitization, the intravenous injection of 20, 40, 60, 80 and 100 c.c. of polyvalent antidysenteric serum on successive days. It would not be safe to carry out this treatment except under hospital or nursing-home conditions, and certainly a supply of adrenaline solution and a suitable syringe should be immediately available in case of sudden anaphylactic collapse. Opinions on the merits of this treatment are divided, remarkable successes having been reported and also many failures. There seems no reason to doubt that a few cases of genuine bacillary dysentery may be followed by extensive ulceration of the whole colon (although the brunt of the infection generally falls on the descending and sigmoid colon), and these may constitute the main successes. It is possible also that the foreign serum-protein may have some non-specific effect. It would be more likely, on pathological grounds alone, for ulcerative colitis to be the result of amœbic dysentery, but this disease must be very rare in Britain. Nevertheless, one of us has himself demonstrated the presence of typical *Entamœba histolytica* in the portal capillaries of a patient who died of "ulcerative colitis" after an illness of six months. This man had never been out of Britain, but worked in contact with men who had been in the East during the war. If any suspicions arise from the clinical history it could do no possible harm to try the effects of a course of emetine injections (see Amœbic Dysentery, p. 254).

*Bargen's Serum.*—Treatment with a serum or vaccine prepared from a micro-organism isolated by Bargen, in America, and believed by him to be the specific cause of the disease, had a transient popularity. The results have, however, been disappointing, and Bargen's serum and vaccine are now rarely used in this country.

It may be emphasized, in conclusion, that the treatment of chronic ulcerative colitis is often disappointing, and the mortality rate, even with the greatest nursing care, is relatively high. Relapses are common after apparent cure, but there is no doubt that complete restoration to permanent health may be attained.

In a few cases the disease assumes a really chronic form, and then strictures of the colon and polypoid overgrowth may arise. Both of these conditions are very liable to malignant change, and colectomy may then be the only possible choice in treatment.

Even after the disease appears to be cured, further treatment must be continued. Stricture (sometimes multiple) of the rectum may require careful periodic dilatation with bougies, and, to guard against the well-known tendency to relapse, dietetic precautions should be relaxed very slowly. A body-belt of silk and wool should always be worn round the abdomen. Purgative drugs must never be employed, but the bowels should be kept regular by suitable diet and the use of liquid paraffin when required.

### DIVERTICULOSIS AND DIVERTICULITIS

*Diverticulosis.*—This is a common condition in adults who have suffered from habitual constipation, or from some acute inflammation of the colon such as dysentery. Its existence is frequently discovered accidentally during an X-ray examination of the bowel for some other purpose. Under such circumstances it is best to tell the patient nothing about it, or to say simply that the colon is not diseased but not quite normal. The early stages

of diverticulosis are symptomless. Later, when the pockets or diverticula are fully formed, symptoms may again be entirely absent; but in a certain number of patients the condition leads to complaints of headache, flatulence and colicky pains in the abdomen. Constipation is almost invariable, but occasional attacks of diarrhoea supervene.

Treatment is directed, when symptoms require it, first to the general health of the patient, and second to the almost invariable constipation. Purgative drugs must never be given, but liquid paraffin is always employed. A low residue diet as for chronic ulcerative colitis (see p. 578) may also prove of service. Other methods of treatment occasionally of value are the rectal administration of a warm douche of normal saline solution, or an enema of warm olive oil run in very slowly at night. Following the latter treatment an absorbent pad must be fixed between the thighs.

**Diverticulitis** or inflammation of a diverticulum is fortunately comparatively rare, but may be a troublesome problem in diagnosis. The early symptoms are intermittent colicky pain, generally in the left iliac fossa but sometimes elsewhere, with fever, and later an indefinite tender mass is felt. Perforation, with generalized peritonitis or fistula between bowel and bladder, may occur and require surgical intervention, but in the great majority of cases the inflammation and local peritonitis slowly settle down after expectant treatment and general sedatives.

### IDIOPATHIC STEATORRHOEA

*(Non-tropical sprue. Gee-Thaysen's disease)*

This is a condition of unknown ætiology in which there is a disturbance of absorption from the intestine. It is claimed by some that it merely represents the adult stage of coeliac disease (p. 297); by others it is held to be a primary disease in the adult. The treatment of idiopathic steatorrhœa differs in no important respect from that of tropical sprue, the details of which are given on p. 257.

### INTESTINAL OBSTRUCTION

The obstruction may be partial or complete, acute or chronic, and may affect any part of the small or large intestine. The causes, as described in textbooks, are commonly divided into those arising in the bowel itself (tumours, malignant and non-malignant, gall-stones, hard fæcal scybala, foreign bodies) and those arising outside of the bowel (herniæ, adhesions and bands, peritonitis). As a rule the obstruction is mechanical, but more rarely is due to paralysis, spasm or peritonitis. Strangulation, volvulus, and intussusception are well-known special varieties of acute intestinal obstruction. Tumour growth is the commonest variety of chronic obstruction in adults.

The recognition of obstruction is not difficult, but exact diagnosis both of cause and site is far from easy, although it does not concern us here.

Once the diagnosis of intestinal obstruction has been made, particularly of the acute variety, surgery is almost always indicated, but there are some important medical aspects of treatment.

The higher the acute obstruction in the intestine the greater the danger, and the more intense are the symptoms of vomiting, cramps, shock and dehydration. These, if they persist, are followed by paralysis of the bowel.



In spite of much observation on patients, and experiments on animals, the reasons for a fatal issue in acute intestinal obstruction are still far from clear, and because of this our rational therapeutics is limited. It is certain that several factors are at work, including the following:—

1. Overdistension of any hollow viscus is known to produce serious effects.
2. It is known that in a closed loop of bowel in animals, some substance is produced which, on injection, causes splanchnic paralysis.
3. Loss of water and of sodium chloride occur from the vomiting.
4. Loss of blood from the general circulation takes place due to great dilatation of the splanchnic vessels.

The surgeon alone can remedy the first two of these, the third is treated by continuous intravenous injection of normal or hypertonic (p. 930) saline until chlorides reappear in the urine; the fourth is dealt with by blood transfusion, followed by immediate operation.

In all cases of suspected acute intestinal obstruction, purgatives must never be used, but if the colon is not involved the lower bowel should be cleared with a simple soap and water enema. When the diagnosis of obstruction has been fully made, and preparations for surgery begun, it is legitimate to use morphia for the intense pain. Fæcal vomiting greatly distresses the patient and the stomach may be washed out with warm water through a small stomach tube.

When the colon is involved, the anaerobic gas-forming bacilli begin at once to play a large part in the issue, and anti-gas-gangrene serum (*B. welchii*) should be administered intramuscularly in doses of 25 c.c. or more.

## MEGACOLON

(*Hirschsprung's disease*)

Hirschsprung's disease is the term generally used to describe megacolon in children. In the adult, megacolon consists of a uniform dilatation of the rectum and sigmoid colon and at times of the entire colon, unaccompanied by any obstruction. The only certain means of diagnosis is by means of a barium enema, and 5 to 10 pints may easily be required to fill the colon.

The ætiology is believed to be a disturbance of the nervous mechanism of the anal sphincter, congenital in origin.

Constipation is the chief symptom, and scybala may lead to stercoraceous ulceration of the bowel.

When recognized in adult life, it is often remarkable how little the condition interferes with health, and the condition may only be discovered when the patient complains that larger and larger doses of purgatives are required to mitigate the constipation which has troubled him from childhood.

It is frequently stated that purgatives are inadvisable, but one of us has seen several examples of megacolon in which very large doses of simple purgatives enabled the patient to empty the bowel, and good health was maintained. An occasional large enema is often required. Hurst strongly advised the systematic use of a conical rectal bougie to overcome achalasia of the rectal sphincter, and this is undoubtedly a good form of active treatment in adults. Recently, various forms of lumbar sympathectomy have been tried in children with the object of reducing the tonus of the anal sphincter. Success has been claimed, but the operation has various dis-

advantages, such as the possibility of sterility. The colon is generally greatly elongated in addition to being dilated, and hypertrophy and extreme redundancy of the sigmoid loop occasionally lead to serious complications such as volvulus. Operation is then the only remedy, but the operative risk is considerable.

### DIETS FOR INTESTINAL DISEASES

#### SPECIMEN DIET AND RULES FOR CHRONIC CONSTIPATION

##### *Rules—*

1. Regular time for meals.
2. Regular, unhurried time for emptying bowels.
3. No cathartics or medicines, unless ordered by physician.
4. Regular exercise, as prescribed.

##### *Breakfast—*

Any fruit—fresh, cooked or dried.	Porridge and milk.
Wholemeal bread and butter.	Marmalade, jam or honey.
Coffee, with milk and sugar according to taste.	

##### *Lunch—*

Soup. Any fish, meat (with fat) or eggs.  
 Vegetables—celery, lettuce, spinach, cabbage; or green salads with mayonnaise.  
 Fresh, preserved or stewed fruits.  
 Wholemeal bread and butter.

##### *Tea—*

Weak tea, milk and sugar.	Wholemeal bread and butter.
Ryvita biscuits.	Treacle scones, treacle gingerbread.

##### *Dinner (as Lunch).*

*Fluids*—in abundance. One tumblerful of hot water on rising, and up to eight tumblerfuls daily. Beer, cider and table waters may all be used.

*Avoid*—White bread, potatoes and strong tea.

Carbohydrate	.	.	.	.	321 gm.	} approximately.
Protein	.	.	.	.	87	
Fat	.	.	.	.	128	
Calories	.	.	.	.	2,784	

#### DIET PROVIDING ADEQUATE BULK BUT AVOIDING COARSE RESIDUE

(Applicable in Spastic Colon and some forms of Constipation)

##### *Early a.m.—*

$\frac{1}{2}$  pint water flavoured with strained orange, lemon or grapefruit juice.

##### *Breakfast—*

Well-strained porridge or cornflakes.  
 Two eggs, boiled, poached or scrambled; or white fish or smoked haddock; or crisp bacon.  
 White bread or Hovis bread—not new—crisply toasted.  
 Butter, honey or golden syrup.  
 One cup weak tea, with milk and sugar.

11 a.m.—

Fruit drink: strained orange juice or grapefruit juice— $3\frac{1}{2}$  oz. (100 gm.).

Water to  $\frac{1}{2}$  pint.

*Lunch or Dinner* (these may be transposed)—

Cream soup.

White fish, chicken, tripe, sweetbreads, tender liver, fillet steak or chop.

Gravy or white sauce without parsley.

Creamed potato. Sieved vegetable.

Curds, custard, jelly, fruit whips, baked apple or soft stewed fruit, without skin or pips.

Cream cheese, water biscuits and butter, if desired.

*Tea*—

Vita-wheat or Hovis bread (not new).

Tomato pulp or Marmite sandwiches.

Plain or Madeira sponge cake. Butter, jelly or treacle.

One cup freshly made weak tea, with milk and sugar.

*Dinner*—

Any two courses from Lunch. (These two meals may be transposed.)

Carbohydrate . . . . .	320 gm.	} approximately.
Protein . . . . .	127 "	
Fat . . . . .	145 "	
Calories . . . . .	3,033	

#### DIET IN CONTINUED DIARRHŒA AND ULCERATIVE COLITIS

*Breakfast*—

Two or three rashers lean bacon, grilled and drained of fat, or grilled white fish, or a lightly cooked egg.

One or two slices crisp toast, buttered sparingly.

Jelly, marmalade or honey.

Freshly made weak tea with sugar and milk.

11 a.m.—

Marmite made with skim milk; or diluted fruit juice, particularly lemon juice with glucose.

*Dinner*—

Large helping tender, lean meat or white fish *finely divided*.

Liver once or twice weekly.

Small helping sieved carrot, spinach, beetroot, flower of cauliflower, asparagus tips, or tomato juice.

Few fingers crisp toast—later, baked or mashed potato.

Baked or puréed apple or lemon or orange sponge or jelly; or curds, or custard, or milk or egg jelly.

St. Ivel or cream cheese with crisp biscuits.

*Tea*—

Crisp toast, rusks, crisp breakfast biscuits or other plain biscuits, or sponge fingers; butter very sparingly.

Jelly, honey or Marmite.

Freshly made weak tea with sugar and milk.

*Supper—*

Average helping meat, etc., as at dinner, or one egg lightly cooked.  
 Fairy toast or rusks with very little butter.  
 Skim milk with Marmite.

*Daily—*

1 pint skim milk.

$\frac{1}{2}$  oz. butter.

Fat should be gradually increased, first increasing butter, and substituting whole milk for skim.

Fat soluble vitamins in the form of concentrates should be added.

To begin with, the patient may not be fit for this amount of food. In this case it is best to start with a diet of rusks, fairy toast, shredded beef, white fish, beef tea and Marmite, gradually adding to the diet until this stage is reached.

## LIGHT DRY DIET IN FLATULENT DYSPEPSIA

*On Waking—*

Tomato juice—1 oz. in 2 oz. water.

*Breakfast—*

Egg or white fish.

Rusks or one thin slice crisp toast buttered cold.

## 11 a.m.—

Cup of Marmite, preferably made with milk (5 oz.).

*Lunch or Dinner (these may be transposed)—*

Tender steak or lean meat or white fish.

Sieved spinach, carrot.

A very small helping of mashed potato.

Curds or milk jelly.

*Mid-afternoon—*

3 oz. warm water flavoured with lemon juice.

*Tea—*

Cream cheese, e.g., St. Ivel.

One slice crisp toast buttered cold.

Water biscuit or tea biscuit or small piece plain sponge.

*Dinner—*

As Lunch, but smaller serving of vegetable and potato.

## 8 p.m.—

Milk or milk and cream—5 oz.—to drink. One tea biscuit.

The following should be avoided:—

*N.B.*—Drinking with solid food.

Soups, gravies, coffee, strong tea, cocoa.

Pork, duck, goose, sausage, pies, herring, kippers and sardines.  
 Green vegetables (except sieved spinach and flower of cauliflower),  
 turnip, peas, beans and lentils.  
 Fruit: at first sugar, glucose, jam, jelly, honey.  
 Bread (do not eat bread at evening meal).  
 Porridge, new bread, hot toast, scones, fruit cakes, pastry.  
 Suet puddings, steamed puddings, milk puddings.

### *Take Daily—*

Milk:  $\frac{1}{2}$  to 1 pint should be used daily. Add cream whenever possible.  
 Butter.

1 oz. tomato juice, lemon juice or 1 oz. orange juice if tolerated.

Ripe banana mashed may be taken, or baked apple pulp.

Carbohydrate	.	.	.	.	95 gm.	} approximately.
Protein	.	.	.	.	70 "	
Fat	.	.	.	.	75 "	
Calories	.	.	.	.	1,335	

### PULPED APPLE DIET

(In severe diarrhoea and ulcerative colitis)

150 to 175 gm. of peeled, raw, ripe, grated apple pulp seven times daily at intervals of two hours.

### *First Day—*

150 gm. of apple pulp, two-hourly, from 8 A.M. to 8 P.M.

Total, 1,050 gm. Carbohydrate, 158 gm. Calories, 632.

### *Second Day—*

175 gm. of apple pulp as before.

Total, 1,225 gm. Carbohydrate, 183 gm. Calories, 732.

This diet may be continued for three to four days, or the following may be substituted :—

### *Breakfast, 8 a.m.—*

Crisp fingers of toast.

Cup of Marmite.

### *2 p.m.—*

175 gm. apple pulp.

### *4 p.m.—*

2 oz. white fish.

Crisp fingers of toast.

### *10 a.m.—*

175 gm. apple pulp.

### *6 p.m.—*

175 gm. apple pulp.

### *12 noon—*

Clear broth.

2 oz. lean meat.

Crisp toast.

### *8 p.m.—*

Marmite or clear broth to drink. Crisp toast.

Carbohydrate	.	.	.	.	125 gm.	} approximately.
Protein	.	.	.	.	35 "	
Fat	.	.	.	.	10 "	
Calories	.	.	.	.	730	

J. W. McNEE.  
 D. SMITH.

# DISEASES OF THE LIVER, GALL-BLADDER AND BILIARY TRACT, PANCREAS AND PERITONEUM

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## DISEASES OF THE LIVER

**T**HE liver is the largest glandular organ and the main chemical laboratory of the body. Physiologists describe it as the chief seat of "intermediate metabolism" from its position in relation to nutrition. It receives through the portal vein all the substances absorbed from the intestine which are required for our bodily activities. The first stage of metabolism consists in the digestion of our food, chiefly by the gastric and pancreatic secretions. The intermediate stage occurs in the liver, where many complex chemical processes of degradation and synthesis take place within the polygonal cells; the mechanism of some of these changes is fairly well understood, but of others is still unknown. The third stage is the transfer, by the blood and lymph, of the nutritive substances prepared in the liver to every cell of the body to provide for its growth, health and functional activity.

There must be many disturbances of the normal working capacity of the liver, unassociated with recognizable structural change, which are still unidentified. Some of these may arise in the liver itself, while others are due to deficiencies, either in quality or quantity or both, in the materials brought by the portal vein from the intestine. Inadequate amounts of certain vitamins in our food, for instance, give rise to a whole series of nutritional diseases; and defective absorption through a diseased intestine may deprive the liver of essential needs.

Everything carried in the portal vein from the intestine must pass through the liver; and this not only includes the requirements for nutrition (mentioned above and derived from our food) but also "poisons," using this term in its broadest sense. These include viruses, bacteria and their toxins, heavy metals, drugs and their alkaloids, organic solvents used in industry and many others. The liver always attempts to destroy, or inactivate, or change into some innocuous compound or simply to immobilize and store all such poisons. This is called the detoxifying function of the liver, and in carrying out this very important protective action the liver is often severely damaged and therefore becomes "diseased."

The liver, moreover, unlike other organs, can be damaged from another direction; for although most of its blood comes through the portal vein it has a second supply from the systemic circulation by the hepatic artery. All general acute infections or "poisons" which have entered the body through, for instance, the respiratory tract, or drugs injected parenterally, may damage the liver when carried there in the arterial stream.

As the liver is so essential and yet so vulnerable, nature has provided for its safety in two very positive ways, both of which are of fundamental importance and have a profound bearing on rational treatment:—

- (a) There is a great excess of hepatic tissue over our normal needs. The major part of the liver may be destroyed by poisons or by tumour growth and yet sufficient remain to carry out perfectly, although naturally with less reserve-power, all the requirements of the body.
- (b) The glandular cells of the liver, and the bile-duct system draining them, have extraordinary powers of regeneration and repair, unsurpassed by any other organ. Thus a liver which has been severely and acutely damaged may later be found to contain large masses of newly formed glandular tissue (nodular hyperplasia), active in function and with a complete system of bile-ducts. It is only when damage has been progressive, as in cirrhosis (*q.v.*), that the power of regeneration is lost and fibrous tissue fills the gaps.

### THE PRINCIPLES OF TREATMENT

A complete realization of the facts mentioned above is necessary when considering the prevention or treatment of hepatic disease. As in other organs, diseases of the liver may be functional (unassociated with recognizable structural change) or organic (associated with pathological changes), and one of these may follow the other.

Many forms of functional disorder of the liver await recognition, and until then all questions of their treatment must be deferred. Insulin enables us, in diabetes mellitus, to control the storage and mobilization of glycogen; and in pernicious (Addisonian) anaemia, when the hepatic store of the factor necessary for the maturation of the red blood cells is depleted, we can replace this by liver therapy. Evidence has long been accumulating that the liver plays an important part in the mechanism of blood-coagulation, and the discovery of vitamin K (p. 512), by means of which prothrombin deficiency in biliary diseases can be prevented or cured, marks a notable advance in treatment. There are now strong grounds for belief that the liver is the main site of manufacture of the plasma proteins, but we do not know yet any certain means of restoring them to normal when diminished and so preventing oedema.

Nutritional deficiencies have recently attracted much attention as possible causes of organic disease of the liver. The new work depends almost entirely on experiments in small animals, especially rats, but some suggestions for preventive and curative treatment have already been made. These are referred to briefly in the sections on acute hepatitis and cirrhosis. It is appropriate here simply to describe the general principles underlying this new experimental approach to hepatic disease and its treatment.

Under experimental dietetic conditions in animals two different kinds of severe hepatic damage have been induced: (1) an acute necrosis coming on fairly quickly and resulting either in death or in subsequent scarring and nodular hyperplasia; (2) a slowly developing diffuse fibrosis or cirrhosis. Both lesions have been proved to arise essentially from a deficiency of proteins or of some of their constituent amino-acids, especially cystine and

methionine. In the necrotic lesion (Himsworth and Glynn) the damage to the glandular cells appears to be direct; whereas the diffuse fibrosis (Best and his colleagues) is preceded by fatty infiltration of the liver cells.

These experiments naturally suggested a trial of proteins, and especially of the amino-acids cystine and methionine, in the prevention and treatment of hepatic disease. In established disease the results so far are briefly recorded. The great possibilities for prophylaxis remain as yet unexplored, not only in individual patients but in many tropical lands where protein deficiency is rife and hepatic cirrhosis very common.

Organic diseases of the liver, with structural alterations in its histology, form the bulk of those to which names are given in medical textbooks. If congenital abnormalities, tumour growth and parasitic infestation are excluded, the remainder all show in their pathology the response of the liver cells to injury of various kinds, and for practical purposes are conveniently included under the term *hepatitis*. The special treatment of various types of hepatitis is dealt with later.

### JAUNDICE

Jaundice, often spoken of as if it were a disease in itself, is simply a common feature of many disorders of the liver. When present, however, it not only alters the clinical picture but may profoundly modify treatment in various ways. It is necessary, therefore, to discuss briefly how it may arise, its effects on the body and the symptoms which may result from its presence.

Jaundice is the evidence of disturbance of one hepatic function, namely, that concerned with the production and disposal of the constituents of the bile; but it may occur in a variety of ways. The bile is a composite fluid, normally containing, in addition to water, three important constituents and mere traces of others. Further constituents are added when the gall-bladder is inflamed but these are referred to subsequently.

The three main constituents in bile are as follows:—

*Bile-salts* are apparently manufactured in the liver alone and are a true secretion. They have an important function in the digestion of fats in the intestine.

*Cholesterol* exists in the bile as “free” cholesterol in contrast to the blood-cholesterol, four-fifths of which is bound as cholesterol-esters of higher fatty acids. In passing through the liver cholesterol is de-esterized, which indicates some physiological activity of the liver apart from mere excretion. The functions of cholesterol in the metabolic activities of cell-membranes and in the blood-plasma are still imperfectly understood in spite of much research, but in liver disease the importance of this substance in relation to the formation of gall-stones is evident enough.

*Bile-pigment (bilirubin)* is a pure excretion product which passes out in the fæces and for which the body has no further use. It is the iron-free part of the hæmoglobin molecule, derived from the breaking-down of red blood corpuscles within cells of the reticulo-endothelial system. Contrary to former beliefs, it is now recognized that the liver is not concerned with its manufacture but merely with its excretion.



Although the least important physiologically of the constituents of the bile, being simply a waste-product, it is the bile-pigment which gives rise to the characteristic yellowness of the skin and tissues in jaundice.

It may be pointed out here, however, that according to modern views jaundice is not necessarily associated with yellowness of the skin, but is synonymous with *bilirubinæmia*—that is to say, an increase of bile-pigment in the blood. Bilirubinæmia must occur before clinical jaundice supervenes, and may often have disappeared when the skin and tissues are still dyed yellow. This point is of major importance in clinical work, for some well-known diseases in which jaundice was formerly considered universal are now known to occur without signs of clinical jaundice at all unless the blood is carefully examined for excess of bilirubin. This is important not only in connection with diagnosis, but also affects treatment indirectly and at times directly.

There have been many classifications of jaundice, none of them perfect because of our limitations in knowledge. The writer still prefers the simple one given below, because it gives straightforward indications of the main facts in ætiology, and therefore of preventive or curative treatment of the underlying cause.

*Obstructive Hepatic Jaundice* arises from obstruction to the outflow of bile either within the liver itself or in the extra-hepatic biliary tract. In this variety all three main constituents of the bile are retained in the blood, and either deposited in the tissues or excreted by some abnormal route. In both circumstances, effects may arise from the jaundice alone which require treatment.

*Toxic and Infective Hepatic Jaundice* is by far the commonest type, and occurs in all forms of hepatitis or damage to the liver. Here again the three main constituents of the bile may, for a time at least, be retained in excess in the blood and give rise to the same problems before and during their excretion.

*Hæmolytic Jaundice* occurs in conditions of excessive blood destruction and is dealt with under the anæmias (p. 488). The jaundice of itself involves no special problems of treatment, since the metabolism and excretion of neither bile-acids nor cholesterol are deranged.

### TREATMENT OF HEPATIC DISEASE

This may be divided into four sections, but these of necessity interdigitate and a strict separation cannot always be adhered to:—

1. Prophylactic treatment.
2. General treatment, applicable to most hepatic diseases.
3. Special treatment, applicable in individual diseases.
4. Symptomatic treatment.

**Prophylactic Treatment.**—This consists largely in the protection of the liver against known “poisons” or substances which damage it, including even drugs used therapeutically. Entry into the body of some “poisons” such as bacteria and their toxins cannot be prevented, but nowadays their ill-effects may often be greatly reduced by the correct use of sulphonamides, penicillin or anti-sera as described elsewhere throughout this book. Some

drugs such as the arsphenamine compounds, cincophen (phenyl-quinolinic acid; quinolan; atophan), must be given in spite of their known tendency to damage the liver, but cincophen especially must be used with care. Gold salts (as used in tuberculosis and rheumatoid arthritis), phosphorus, santonin and carbon tetrachloride (used for parasitic worms), trinitrotoluene (used for explosives), tetrachlorethane (used as "dope" for aeroplane wings), and many other "solvents" now used in industry are all liable to cause severe liver damage. The general question of susceptibility in liver disease is too difficult to assess and our knowledge too meagre, but certainly anyone who is known to have suffered from jaundice, or from a disease which might injure the liver such as acute infective hepatitis, syphilis, malaria, yellow fever, Weil's disease or chronic alcoholism, should be employed with care in chemical industries and, if occasion arises, treated circumspectly with certain drugs.

Certain important prophylactic measures arise in connection with cirrhosis (*q.v.*), but these are dealt with fully under that heading.

**General Treatment.**—In this section it is assumed that the liver is already damaged, or in the ordinary sense "diseased." Rational treatment is essentially founded on the two fundamental points mentioned earlier, namely, that the body is provided with a great excess of liver tissue over normal requirements and that such liver cells as remain intact have extraordinary powers of regeneration and repair. Our aim in general treatment, therefore, is to protect and nourish the cells which are undamaged and to tide over the time needed for repair. Differences in emphasis naturally arise in the application of adequate therapeutic measures for acute or chronic conditions, but the main principles remain the same.

*Rest in bed* will diminish many of the metabolic activities of the liver, lessen the call on the glycogen store and so help to protect the undamaged liver cells.

*Warmth* is provided by rest in bed, and tends to decrease the increased metabolism induced by cold.

*Glucose* is valuable, especially in acute hepatic disease, to replenish the cells with glycogen and so protect them from further injury. It may be given by the mouth as glucose drinks or injected intravenously, according to the urgency. Further, in all forms of acute and severe damage to the liver the blood-sugar falls and coma may supervene from which, in the earliest stage only, recovery may be as dramatic as after administration of sugar to a diabetic with acute hypoglycæmia from excess of insulin.

*Diet.*—Until recently a diet chiefly carbohydrate in composition was recommended, as throwing least strain on the damaged organ; and it was considered that proteins should be kept down to the minimum bodily requirements since the metabolism of their derivatives requires hepatic activity. Fats were only regarded as contraindicated in obstructive jaundice, in which the bile-salts necessary for their digestion are absent from the intestine. Recent advances in knowledge, however, seem to show that protein restriction is probably wrong and that reduction of fat in the diet has a much wider significance and value than was formerly supposed. The new facts find their fullest application in relation to the prevention and treatment of chronic disease of the liver, and are fully considered in the section on cirrhosis (p. 589). All that need be said here, to prevent repetition, is that protein in adequate amount, particularly in the form of skim milk

—a rich source of methionine—should be given in ample amount except in the early acute stage of hepatic disease. Fat should be definitely restricted, chiefly for the reasons given later. Apart from such reasons, however, it has long been recognized in practice that “cooked fats” are a frequent cause of indigestion and flatulence in liver and biliary disease and all fat allowed should be in the form of milk or butter.

*Drugs*, except the simple saline purgatives, should be used as sparingly as possible, since most alkaloids are finally disposed of by hepatic activity. Restlessness and delirium may be serious problems in the most acute forms of hepatic damage (acute necrosis, *q.v.*), and it may then be essential to use powerful hypnotics such as barbiturates and opium. In such case, glucose should be freely administered to counteract the primary objections to these drugs.

**Special Treatment.**—Many individual diseases in which the liver is seriously involved and jaundice frequent are discussed elsewhere in this work. Among the forms of hepatitis due to infection, all of which involve special prophylactic or curative treatment, reference may simply be made, as examples, to syphilis, Weil's disease (spirochætosus icterohæmorrhagica), malaria, yellow fever, rat-bite fever and amœbic dysentery. In toxic hepatitis due to arsenic, mercury and probably gold, the therapeutic value of B.A.L. (British Anti-Lewisite), p. 812, has been noted as a recent advance.

It is only necessary, therefore, to discuss the special prophylactic or curative measures applicable to some of the common hepatic diseases not dealt with elsewhere.

### ACUTE INFECTIVE HEPATITIS AND HOMOLOGOUS SERUM JAUNDICE

Recent research work seems to show that these two conditions are distinct and separate entities, but their essential pathology and clinical course are so similar and our advances in knowledge concerning them have been so closely linked, that it is convenient to deal with them together.

In Britain, and indeed throughout many parts of the world, an acute sporadic disease affecting the liver and known as catarrhal jaundice has long been familiar in medical practice. Much evidence had accumulated in the last thirty years that the same disease may appear in small epidemics, generally affecting children and young adults, and was obviously infectious. Fatalities were rare, but the few opportunities for post-mortem examinations seemed to show that the essential lesion was a hepatitis and not primarily a catarrh of the larger bile-ducts as was formerly believed. This change of view concerning the pathology clearly indicated a different line of approach to treatment.

In the Second World War acute infective hepatitis broke out in epidemic form among all the belligerents in numbers so large as to affect both military operations and strategy. Intensive research naturally resulted, and the whole status of the disease has been greatly clarified although many gaps in our knowledge remain to be filled. Observations by the new technique of liver puncture quickly confirmed the essential lesion as a true hepatitis. Moreover, the intensive studies soon widened to include other forms of acute

hepatic damage, some known in the past but never understood and others thrust into unexpected prominence by the circumstances of war. These included, one after another, the sudden outbreaks of jaundice long known to occur, but never adequately explained, in clinics where many patients were receiving injections of salvarsan compounds; second, the tremendous incidence of jaundice, particularly in American troops, following injection of prophylactic yellow fever vaccine containing human blood-serum as an essential ingredient; and, third, the unwelcome occurrence of jaundice after transfusion of wounded or injured men with certain batches of "pooled" human whole blood or plasma. In the last two, the common factor was the administration by injection of human plasma, and a similar acute hepatic disorder had been noted rarely, years before the war, after the use of measles and mumps convalescent sera in prophylaxis. The suspicion that outbreaks of jaundice in V.D. clinics fell into the same category was at once aroused, and it is now generally accepted that imperfect cleansing and sterilization of syringes and needles used for batches of patients may spread the disease (see p. 214). All of these matters are of obvious importance in preventive treatment.

The disease occurring spontaneously both in peace and in war is now generally known as *Acute Infective Hepatitis*. The disease which follows the injection of human blood or plasma has been named *Homologous Serum Jaundice*.

The question arises, and might obviously be important some day in treatment, whether these two conditions are not really the same disease, in one case transmitted naturally and in the other, so to speak, unnaturally. Both are believed to be virus infections, but whereas acute infective hepatitis has a regular incubation period of about 28-30 days, homologous serum jaundice does not develop for, on an average, about 90 days. Human transmission experiments have been carried out successfully, but so far no one has reported a change of incubation period in the volunteers; and recent work, which requires confirmation, suggests that the one disease does not confer immunity against experimental infection with the other.

The preventive treatment of homologous serum jaundice is self-evident, but with the rapid development of blood transfusion as a remedy, and of blood banks issuing "pooled" blood or plasma, the difficulties are great. No one knows how long the virus may persist in an apparently healthy donor's blood, and the only precaution possible at present is careful inquiry about previous jaundice in all potential blood donors.

The preventive treatment of acute infective hepatitis has advanced a little further. It is known, from transmission experiments, that the virus is present in the faeces, and there was the clearest proof of contamination of a water supply in one well-known summer-camp epidemic in America. This would not explain, however, the short exposure to infection, *e.g.*, one day's proximity at school, so frequently noted (Pickles) in rural areas where contact is easily traced, and it is evident that the disease must be transmitted frequently in other ways. "[Droplet infection and spread by flies have both been suggested, but proof is lacking."

One thing is certain and of considerable practical importance. The infectivity of the disease is greatest during the invasive period before jaundice is visible, and thereafter rapidly declines. In the Service hospitals during the war few of the nurses, doctors or orderlies in daily contact with many

jaundiced patients contracted the disease. It seems evident, therefore, that during the later stages of the disease strict isolation is unnecessary.

No specific treatment is available for acute infective hepatitis, and since it is a virus disease sulphonamides and penicillin are useless. All that is required is the realization that the damaged liver will quickly regenerate and return to normal in the great majority of cases under the general treatment previously described. Attempts have been made to influence the course of the disease, and especially to shorten it, by administration of the sulphur-containing amino-acids cystine and methionine, but no very successful results have been achieved.

In a very few patients complications arise, both of which alter prognosis and treatment. It is well known that in the course of an ordinary and apparently benign attack of acute infective hepatitis the clinical picture may quite suddenly alter for the worse, with the onset of the most dreaded form of hepatitis discussed below, namely, acute necrosis (yellow atrophy) of the liver.

Further, it is now recognized that recovery from the acute damage is not always complete, and a small number of cases progress to a subacute stage and even to a typical cirrhosis.

#### ACUTE (AND SUBACUTE) NECROSIS OF THE LIVER

*(Acute yellow, acute red atrophy)*

The cause of this dreaded but fortunately uncommon hepatic disease is often unknown. It may suddenly arise in the course of acute infective hepatitis, as already stated, or during pregnancy, but frequently starts spontaneously without any previous warning change in the body or its functions. Certain drugs, especially cinchophen (atophan) and arsenic are, however, recognized as positive ætiological factors, while solvents used in industry (especially if they contain the benzol-ring in their chemical structure) have also been implicated. The possible ætiological significance of the necrosis resulting from protein-deficiency experiments in animals is still unknown.

When the necrosis of liver cells is sudden and very extensive so that liver function totally fails, nothing can be done for the patient. The only clinical hope is that sufficient cells may be left alive to allow of regeneration, and glucose administration should be adequate and continuous. Insulin is often recommended along with the glucose, but there is no clear evidence that this is essential. Delirium is often most violent in the early stages, and one nurse may be quite unable to control the patient. Powerful hypnotics such as morphine, which are in principle contraindicated, may be required but are often without great effect. Finally the patient may sink into coma, and glucose (which it may have been impossible to administer during the height of the delirium) should then be given freely by the intravenous route, without, it must be admitted, great expectations.

In subacute necrosis, in which more liver cells survive and in which nodular hyperplasia may supervene, the prognosis is better and adequate hepatic function may be restored for a number of years. The treatment in the earlier stages is the same as for acute necrosis, but later approximates more closely to that which is described in connection with the prevention of cirrhosis.

**CIRRHOSIS OF THE LIVER***(Chronic interstitial hepatitis)*

This is still one of the commonest chronic hepatic diseases. The essence of the pathology is the effects of progressive damage to the liver cells, which for a time continue to exhibit their remarkable powers of regeneration. Finally, the power of repair is overcome, fibrous tissue fills the gap, and small areas of glandular cells are left isolated amidst the increasing scar tissue. The bile ducts and portal blood capillaries undergo extreme distortion and compression in the contracting fibrous tissue, leading to the well-known signs of portal obstruction. Blood continues to be supplied to the liver through the hepatic artery, and the quantity may even be augmented by dilatation of the artery. Finally the functions of the organ totally break down and death results. It must be remembered that when portal obstruction is well marked the absorbable products from the intestine, which would normally be dealt with in the liver, escape directly into the systemic circulation by collateral veins and lead to some of the disturbances of metabolism common in hepatic cirrhosis.

Once the clinical features of cirrhosis of the liver are fully established, only palliative treatment is possible, but even then much can be done to prolong the life of the patient and relieve some of the most trying symptoms.

**Prevention.**—The real treatment of cirrhosis is preventive; or, failing this, the early recognition of the onset of a chronic hepatitis before the regenerative powers of the organ have been seriously impaired. This at once raises the question of aetiology, an old clinical puzzle in the solution of which considerable recent progress has been made. The writer, from a very considerable experience, has no doubt that in Britain, up to the Second World War, alcoholic excess was by far the commonest causative factor in cirrhosis; but the vast numbers of cases of acute infective hepatitis in the Services and civil population during the war, some of which have already progressed to chronic hepatitis, may well make this the most important aetiological factor in the years to come. It has long been known that cirrhosis may occur in total abstainers, and some of these patients may quite probably have suffered in the past from unrecognized acute infective hepatitis or "catarrhal jaundice" without actual icterus. Moreover, the question of how alcohol injures the liver has been much disputed—is it a direct action or only indirect through the accompanying chronic gastritis, enteritis and anorexia resulting in a nutritional deficiency?

The recent experimental work on animals, already referred to, suggests that the second view is correct and that chronic alcoholism, which is well known to be associated with a fatty liver, may finally end, through defective absorption of protein from the damaged intestine, in cirrhosis.

Preventive treatment in some tropical lands where protein deficiencies in the diet are constant and cirrhosis is common, even in children, has not so far been attempted. A loop-hole must at present be left for chronic hepatitis resulting from parasitic infestation, especially schistosomiasis; but here again the addition of a nutritional defect may be necessary for the full development of the disease.

**Early Cirrhosis.**—If, in Britain, a diagnosis of pre-cirrhotic hepatitis *due to alcoholism* can be made early enough, *complete* cure can, as a rule, be promised

under a suitable régime of simple treatment and total abstinence. In the well-to-do the typical patient with hepatic cirrhosis is seldom a solitary drinker or dipsomaniac and is not a "martyr to delirium tremens," but more often an individual who imbibes too much alcohol because he likes conviviality, and who generally also takes too much food and too little exercise. In hospital patients, on the other hand, an occupation implying easy access to alcohol—barmen and barmaids, employees of breweries, etc.—is of much significance. The typical patient in the pre-cirrhotic stage is sallow, has frequent "liver attacks" (of gastritis), and complains of headache, irritability or drowsiness. On physical examination the liver is enlarged, often tender, and piles are a common complaint.

The actual treatment of these patients is simple enough :—

*Teetotalism must be enforced for life*, and the great probability of complete cure, with the certainty of death if advanced cirrhosis is allowed to supervene, must be stressed to the full.

*Rest in bed, warmth, and a restricted diet* until all signs of alcoholic gastritis have gone. Gastric lavage may be essential at first to remove the excessive mucous secretion. The diet should eventually have a high carbohydrate, normal protein and reduced fat content.

*Spa treatment*, properly applied, including a correct dietary régime, baths or packs over the enlarged liver, the mild aperient spa water, and not least the discipline and removal from the temptations which have beset him, is often of the utmost value to the well-to-do patient at this early and curative stage of the disease.

**Advanced Cirrhosis.**—If cirrhosis of the liver, whether following infective hepatitis or alcoholism, is first seen when the liver is contracted, portal obstruction evident, and jaundice and ascites present, then palliative treatment only is available. There is a fairly common belief that once ascites and jaundice have supervened, death is inevitable within about six months. This is quite erroneous, and with careful handling life and moderate health may be prolonged in a number of cases, but certainly not in all, for five years or more.

The treatment in the late stages is similar to that recommended for pre-cirrhotic hepatitis, but rest in bed is best avoided until near the end, or until cedema renders walking impossible. It is difficult in many of these patients to stop alcohol altogether, and no rule can be laid down. A patient, treated by the writer, lived and worked very actively for more than five years after ascites had required tapping, while still consuming a bottle of whisky daily.

*Tapping of the abdomen* should be begun fairly early, before marked cedema of the lower limbs appears, and before breathlessness becomes excessive from the overdistended abdomen. The average amount removed at a sitting from a patient with a moderately full abdomen is 11 to 15 pints. The technique of abdominal tapping is discussed elsewhere (p. 944), but there are some practical points applicable to cases of hepatic cirrhosis which are worthy of mention. Antiseptics should be applied to the stretched and unhealthy abdominal skin with care, especially tincture of iodine, which in the writer's hands has several times produced marked pustulation. Weak picric acid is generally quite suitable, but a good (although gentle) rubbing with rectified spirits is adequate, and probably the safest of all. A fairly large trocar and cannula should be used, simply connected to a fine rubber

tube, and the ascitic fluid is allowed to escape by gravity alone into a basin under the bed and invisible to the patient. After procaine infiltration of the skin and abdominal wall right through to the peritoneum, a short slit made through the skin with a fine scalpel or tenotome allows the trocar and cannula to be inserted through the abdominal wall without undue pressure or jerking.

Although the slit made by the scalpel closes and heals far more readily than the rounded hole which the trocar alone would make, a certain amount of leaking after each tapping is to be expected, and may persist for forty-eight hours. Gauze pads and a binder are therefore generally essential, especially if, as happens in suitable employments, the cirrhotic patient is tapped one day and allowed to return to work the next. It has been found by experience that tapping in the flanks is easier for the patient (and the gauze pads are less obvious) than tapping in the middle line. The slit through which the tapping is carried out frequently appears very red and angry after forty-eight hours, and sepsis may be suspected. In practice, however, sepsis very seldom occurs, and there need be no fear, whether the puncture continues to leak or not, of sepsis spreading into the abdomen. The frequency of tapping varies greatly in different cases. At first this small operation may be required once a week, but later (possibly due to adhesions or to peritoneal thickening providing additional collateral vessels) tapping may be needed only at intervals of four to six weeks or more.

*The Talma-Morison Operation.*—This is carried out by surgeons in different ways, the aim in all operations being to increase the collateral circulation of the blood and relieve portal obstruction. The operation should always be preceded by tapping the abdomen. The peritoneal surfaces covering the liver and diaphragm are rubbed with gauze or scraped to induce adhesive inflammation, and the great omentum (which is rich in veins) may be similarly dealt with, or brought out through an opening to lie beside the rectus abdominalis muscle and securely fixed there.

The results of this operation are difficult to assess, as it has generally been carried out only in the last stages of cirrhosis. The writer has only seen great success in one man, who at the time of the operation was still very obese. In this patient the ascites, greatly complicated by obesity, was checked for two years.

*Œdema of the legs and scrotum* is a great source of trouble in the late stages of cirrhosis, just as in chronic cardiac failure. Much turns here on the efficiency of excretion by the kidneys, and if this is poor the end is not prolonged. It is well to recollect that œdema of the scrotum and legs must not be regarded as a "stagnant pool" but that even in the worst cases there is a constant but sluggish flow or movement of the fluid. The use of a "cardiac bed," or, failing this, an inclined plane, so that sudden postural alterations of the limbs can be made from time to time, enhances the movement of the fluid and greatly increases the possibility of control of the œdema. The effects of changes of posture are often amplified to a remarkable degree by the use of mersalyl (1 to 2 c.c. intravenously or intramuscularly), which can be injected with safety twice a week in all cases of cirrhosis unless there is also serious renal disease. The results of combined treatment with mersalyl and rapid postural alterations of the limbs are as a rule so satisfactory that questions of acupuncture, incisions, or the insertion of Southey's tubes will seldom arise.



Recently, diets high in calories and especially in protein-content have been suggested, with the object of raising the level of the plasma proteins and so diminishing ascites and oedema. Intravenous injection of the patient's own ascitic fluid after tapping has been practised for the same reason. Good results have been claimed, but these methods must be regarded as under trial. Apart from a high protein diet the two sulphur-containing amino-acids, cystine and methionine (derived from proteins) have also been administered. This suggestion derives from the animal experiments already mentioned. Neither of the two amino-acids is pleasant to take, their cost is high and their manufacture is still restricted. Few physicians can collect a sufficient number of advanced cases of cirrhosis for a properly controlled trial, but in one series reported in America very good palliative results were claimed from their use. Prolongation of life with reasonable health would be a definite gain, but in advanced cirrhosis no real cure can be expected.

In animal experiments known liver poisons cause more extensive damage when the diet is deficient in vitamin B; yeast or thiamin may therefore be prescribed (see p. 400).

*Hæmorrhage* may occur from various situations—epistaxis, melæna, hæmorrhoids. Bleeding from the rupture of dilated œsophageal veins is fairly common, and may be almost immediately fatal. The symptomatic treatment is similar to that applicable to any severe hæmorrhage. Attempts have been made to inject sclerosing fluids into the œsophageal varices but the results have been disappointing.

*Anæmia* is common in cirrhosis of the liver, especially in the later stages, and quite apart from active hæmorrhage. Its treatment is unsatisfactory and is referred to on p. 485.

*Hiccup* is fairly common in a number of hepatic diseases, due to irritation of the diaphragm, and in cirrhosis it may persist without interruption for days, and completely exhaust the patient. The treatment is difficult and various remedies may be tried in turn—60 gr. (3.6 gm.) of bismuth sub-nitrate, washing out the stomach with water as hot as can be borne,  $\frac{1}{10}$  gr. (1.3 mg.) of atropine sulphate,  $\frac{1}{4}$  gr. (16 mg.) of morphine and finally  $\frac{1}{8}$  gr. (8 mg.) of cocaine by injection.

*Coma*.—It is seldom justifiable to treat the drowsy toxæmic state which precedes the final coma when the liver totally fails. But one point concerning coma in cirrhosis is of some clinical importance. It happens occasionally that laparotomy is performed on a patient in whom hepatic cirrhosis is never suspected until the abdomen is opened. Such patients, following the operation and the anæsthetic, may rapidly sink into deep coma. Glucose should be administered intravenously at once and the otherwise inevitable fatality may be averted. It is best to use 20 per cent. glucose in saline, injected very slowly, and as much as 200 to 300 c.c. may safely be given.

### SPECIFIC INFECTIONS OF THE LIVER

The treatment of syphilis, malaria, amœbic hepatitis (tropical abscess), hydatids and other infections are all dealt with elsewhere.

### SUPPURATIVE PYLEPHLEBITIS, CARCINOMA OF THE LIVER, ETC.

Omitted, as treatment is surgical or impossible.

## DISEASES OF THE GALL-BLADDER AND BILIARY TRACT

There are two common diseases of the gall-bladder and biliary tract: (1) Cholecystitis or inflammation of the gall-bladder; (2) gall-stones. In the majority of cases, but not in all, the second disease is the sequel of the first.

It is important to consider briefly a few points in ætiology, without a knowledge of which it is impossible to understand rational treatment, both prophylactic and curative.

**Microbic infection** is the sole cause of cholecystitis, and the essential cause of most cases of gall-stones. Much discussion has always arisen as to whether the infecting organisms reach the biliary tract from the blood stream and are excreted by the liver with the bile, or whether the route of infection is a direct ascent from the duodenum into the common bile-duct. We possess no strong evidence in favour of one route as against the other. Typhoid fever is the only specific disease notoriously associated with infection of the biliary tract, but although this is an intestinal disease it is also a septicæmia in its earlier stages. A streptococcus is a common infecting organism in cholecystitis, but there is no proof of its intestinal origin, and indeed its presence has always raised the difficult problem of the influence of focal infection (in teeth, tonsils and elsewhere) in relation to the ætiology of cholecystitis and gall-stones. Coliform organisms (including *B. typhosus*) are also commonly found in inflamed gall-bladders, but other organisms such as staphylococci, gas-forming anaerobic bacilli, and diphtheroid bacilli also are met with.

**Biliary stasis** is universally accepted as an important contributory cause of biliary infection. This occurs in pregnancy, and accounts, in part at least, for the frequency of gall-stones in married women. But lack of exercise, a sedentary occupation and obesity are also important in this respect, and require to be remembered in treatment.

**Composition of the Bile.**—The three chief constituents of the bile—bile-salts, cholesterol and bile-pigment—have already been described. When infection occurs, a fourth constituent—calcium—is added, since the inflammatory exudate is rich in lime-salts. Thus the common faceted gall-stones are made up of a mixture of calcium-salts, cholesterol and bile-pigment. The prevention of the addition of calcium to the bile depends simply on the avoidance or cure of infection. Other alterations in the normal constituents of the bile are also important, not in connection with primary cholecystitis, but with some varieties of gall-stones. Pure pigment stones of bilirubin may occur at an early age in acholuric jaundice (p. 489), and their presence in the gall-bladder is frequently followed by infection and cholecystitis. Cholesterol is increased in the bile in pregnancy, obesity and other conditions, and this possibly accounts for the formation of solitary cholesterol gall-stones, which certainly arise in a sterile gall-bladder. Secondary cholecystitis is here again of frequent occurrence. The problem of treating an excess of bile-pigment and an excess of cholesterol is discussed later.

**The Gall-Bladder.**—Both the structure and function of the gall-bladder have important bearings on treatment. The normal gall-bladder wall is thin and almost translucent, but its mucous lining is a complex honeycomb. In chronic cholecystitis the whole wall may become greatly thickened and scarred, and it is evident that the microbic infection lies deep in the wall, and that the presence or absence of micro-organisms, free in the gall-bladder

bile, is relatively unimportant. Obviously no medical treatment, probably not even any drug carried to the thickened gall-bladder wall by the blood stream, can cure this type of infection, and when the gall-bladder wall is thickened and sclerosed surgery is the only therapeutic remedy. If, however, as the writer believes, cholecystitis can be diagnosed early, before permanent changes have occurred in the gall-bladder wall, then medical treatment may effect a cure.

The main function of the gall-bladder is to concentrate the bile, and to empty itself, or more accurately to empty itself partially, when suitable food enters the duodenum. Advantage is taken of this concentrating power in the diagnostic X-ray method known as cholecystography, and advantage of the ability of the gall-bladder to evacuate its contents is made use of therapeutically.

### CHOLECYSTITIS

Acute cholecystitis is of several varieties—catarrhal, suppurative and phlegmonous. The last two are fortunately rare and fall at once into the realm of surgical emergencies.

Catarrhal cholecystitis is exceedingly common, and although it no doubt starts acutely this phase is seldom recognized clinically. It is best to regard it as a mild form of microbic infection of the biliary tract, smouldering slowly with the production of definite clinical symptoms, and, unless cured, almost inevitably ending with the sequel of gall-stones. It will thus be recognized that the preventive treatment of gall-stones is essentially bound up with the problems of catarrhal cholecystitis, the clinical features of which were described by Moynihan as the “inaugural symptoms of gall-stones.”

Various aspects of treatment must be considered—preventive, curative and symptomatic. *Preventive treatment* of the infection must remain unsatisfactory until we know why the various micro-organisms implicated settle in the biliary tract. The well-known occurrence of cholecystitis in the typhoid group of fevers suggests, however, active prophylactic treatment (see below) during the course of these diseases. Catarrhal cholecystitis (and its sequel of gall-stones) is very often associated with obesity, and the removal of this important predisposing cause is dealt with elsewhere (p. 383). *Curative treatment*, directed towards the sterilization of the biliary tract, is only possible in the early stages when the infecting organisms are either free in the bile or have not yet become deeply embedded in a chronically inflamed and thickened gall-bladder wall. Specific methods of treatment include drugs which are known to be excreted by the liver in the bile, or carried in the blood stream to the wall of the gall-bladder. The first method, taking advantage of the chief normal function of the gall-bladder in concentrating the bile, has obvious advantages, and various remedies have been recommended. Hexamine in large doses of 300 gr. (18 gm.) daily (the urine being kept strongly alkaline to prevent irritation of the bladder) is now seldom used. Sodium salicylate, 30 gr. (1.8 gm.) or more three times a day, is recommended by some authorities. Both of these drugs have nowadays been largely superseded by sulphonamides in full doses, which are freely excreted in the bile; their limitations are obvious, however, in respect of sulphonamide insensitive organisms. Penicillin has not proved to be of much therapeutic value.

If the drugs mentioned fail, the writer is of the opinion that the procedure often known as "non-surgical biliary drainage" offers at present the best chance of cure of a catarrhal cholecystitis. This method takes advantage of the capacity of the gall-bladder to contract suddenly and empty its contents, and arose out of the application of a diagnostic test still commonly employed—biliary drainage after the passage of a duodenal tube. It was found that various substances—irritants such as concentrated solutions of magnesium sulphate and more normal stimulants such as olive oil—when introduced through the duodenal tube, at once excited biliary contraction and a free flow of bile. It was soon realized that here was a therapeutic method by means of which the biliary tract could be emptied at will, and the process repeated when the gall-bladder filled again. An important extension of the method soon appeared, which has made it entirely suitable for ordinary clinical use. It was found that either concentrated solutions of magnesium sulphate or olive oil were quite efficient in inducing gall-bladder contraction when given on an empty stomach, and without the need for a duodenal tube at all.

In practice the method of non-surgical biliary drainage is carried out as follows:—

1. The following prescription is made up:—

Magnesium sulphate, 25 per cent. solution in water.

Syrup of lemon—just sufficient to flavour.

One teaspoonful or more (the suitable dose varies, but purgation should be avoided) to be taken in a wine-glass of water, on an empty stomach, immediately on waking in the morning and at least twenty minutes before breakfast.

2. During the day, advantage is taken of the action of olive oil, and *before* the midday and evening meal a dessertspoonful of olive oil should be taken to empty the biliary tract. Olive oil acts also in another important way, referred to below. If unobtainable, it may be replaced by arachis (pea-nut) oil.

This method should be carried out daily and systematically for several months, and later, when all symptoms have disappeared, it should be repeated periodically in short courses.

*Symptomatic Treatment* in catarrhal cholecystitis is mainly concerned with the flatulent dyspepsia which is so common. Cooked fat or fried dishes generally aggravate the condition. Olive oil, however, a natural fat, is the most valuable agent we possess for the relief of flatulence, and when taken before meals ( $\frac{1}{2}$  to 1 oz.) it greatly diminishes the flow of acid gastric juice. Bismuth oxycarbonate and alkalis are also useful in some cases, and are frequently employed.

*Dietetic Treatment* in cholecystitis requires consideration for several reasons. First, the problem arises of whether gall-stones can be prevented by diminishing the cholesterol content of the food, since cholesterol is one of the important constituents of biliary calculi. With this end in view egg-yolk, sweetbreads, kidney, liver, cream, suet and other foods rich in cholesterol have been excluded from the diet, but the writer is not convinced that this can alter in any important respect the amount of cholesterol available to the body from many sources.

*Spa Treatment* is of undoubted value in cholecystitis, not only because of the regular dietetic routine followed, away from domestic or business cares, but also because of the effects of the mineral water, best taken hot and always on an empty stomach. The spa water is generally sipped slowly, while walking about, a pint at a time, and is drunk before breakfast and again in the afternoon.

**Chronic Cholecystitis.**—Chronic cholecystitis may occur either with or without the presence of gall-stones, and the latter condition is dealt with separately.

As has been indicated, when the gall-bladder is chronically inflamed, thickened and sclerosed, and when cholecystography has shown its inability to concentrate bile or loss of its capacity to empty itself, then medical treatment can only be palliative, and in the present state of our resources surgery is the only cure. The palliative methods are the same as those already described.

**Gall-stones.**—Once gall-stones have formed in an infected gall-bladder there is no known method of dissolving them. Very small ones may pass into the intestine, others may block the ducts, and large ones remain in the gall-bladder to set up further inflammation and to be joined by a further collection of stones.

Quacks have for long claimed to dissolve gall-stones, and the method they commonly employ is to administer olive oil in a cachet or enclosed within some form of capsule. As has been indicated, olive oil before meals is our best remedy for the symptomatic treatment of the almost invariable flatulent dyspepsia, and so many of the patients at once experience great relief. The olive oil, given in this way, is converted into a soap, and to the inexperienced person the masses of soap in the stools may bear a fair resemblance to gall-stones, and may be demonstrated to the patient as such. Physicians must be well aware of this trick, and able to explain it to their patients whose symptoms soon return when the treatment is stopped.

At present the only certain cure for gall-stones is their surgical removal, and the physician is chiefly concerned with the following therapeutic problems.

*Biliary Colic.*—As soon as the diagnosis is made this should be treated at once by injection of morphine combined with atropine or with pethidine.

*Exacerbations of Cholecystitis in association with Gall-stones.*—Such attacks are common, associated with fever, vomiting, intense pain and tenderness over the gall-bladder. The clinical problems of treatment are sometimes difficult, but an attempt must always be made to allow the acute inflammation to subside before operation is contemplated. The dangers of waiting are perforation of the gall-bladder and suppuration (empyema of the gall-bladder). Both of these are fortunately rare, and, if they are excluded, treatment should be passive and not active. Pain should be controlled with morphine and atropine or pethidine, but no purgative or other drug which might affect the gall-bladder or biliary tract must be given. Diet must be restricted to fluids such as fruit drinks flavoured with glucose until the acute inflammation subsides in a very few days.

*Pre-operative Treatment.*—Much can be done to increase the safety of an operation for gall-stones. Liver function is always disturbed, and glucose, or fruit drinks, or a combination of both, should always be given freely for some days prior to operation.

Obesity is a frequent source of danger, and few surgeons are willing to operate, except in emergency, on very obese patients suffering from gall-stones. For safety the obesity must always first be treated by the dietetic and other methods described elsewhere (p. 383).

**Conservative Treatment of Disease of the Biliary Tract.**—It happens fairly frequently that patients who are old and infirm, or who suffer from serious disease of other organs (heart, lungs, kidneys, diabetes), develop symptoms which point unmistakably to a disorder of the biliary tract—gall-stones or an acute exacerbation of chronic cholecystitis, or both. Operation, with its grave risks, is imperative immediately only when empyema of the gall-bladder or perforation are diagnosed, and at a later period when completely obstructive jaundice indicates impaction of a stone in the common bile duct. Otherwise every attempt must be made to avoid operation, and, as has been indicated, it is remarkable how acute signs and symptoms of disease of the gall-bladder may settle down within a few days, with rest and administration of morphine. The scope of palliative treatment thereafter to be adopted must vary with the general condition of the patient, and rigid rules may be unsuitable. Nevertheless it is often possible to damp down the biliary troubles of such patients for years, and life may terminate only by the progress of the other disease.

In many of these cases it is advisable to carry out at a suitable time the X-ray examination of cholecystography, and there is generally no contra-indication to this investigation. The information obtained may be negative or incomplete, but may at times be an important guide to the physician and also to the surgeon if an absolute emergency arises.

**Advice Regarding Operations on the Biliary Tract.**—When a patient first suffers from biliary colic or from the first obvious attack of acute cholecystitis, the treatment is medical provided the well-known surgical emergencies can be excluded. When, as generally happens, the acute phase passes over, the physician has time to use the appropriate tests for accurate diagnosis, and to consider his patient in respect of age, general health and obesity. Even when gall-stones or chronic cholecystitis have been identified, it may be entirely justifiable to continue medical treatment in the hope of avoiding subsequent attacks, but each case must be judged on its merits.

When operation is strongly advised the physician may be asked to give his reasons, since medical treatment may control the symptoms and since it is well known that gall-stones may be discovered accidentally at necropsy in patients who have never been known to suffer from biliary disease. Further, the physician may often be asked about the possibility of "dissolving" gall-stones, and will be able to explain the secrets of the olive-oil treatment.

When advising operation the rare possibility of cancer of the gall-bladder (see below) should not be mentioned, and the writer has generally found it best to allude only in very general terms to the serious acute complications (such as empyema and perforation) that may ensue. The patient may be warned that the presence of gall-stones limits his or her activities "geographically." It may be pointed out that emergency surgery in the upper abdomen is serious even when all the resources of a big city are available, and that in the depths of the country, on holidays abroad or on a sea-voyage the risks of an immediate operation are greatly enhanced. Further, the patient should be told that the liver itself, an essential organ for life, is

always injured by the presence of gall-stones and biliary sepsis, and that damage to the heart muscle is not infrequent.

For these reasons, among others, the patient should be strongly advised to seek operation during a quiescent stage of the disease, after all necessary preparative medical treatment has been carried out.

### CARCINOMA OF THE GALL-BLADDER, BILE DUCTS AND PANCREAS

Carcinoma of the gall-bladder is almost invariably associated with gall-stones; but it occurs, however, only in about 4 per cent. of cases. The prophylactic treatment is to remove the gall-stones. Early diagnosis is very difficult, and since the growth rapidly invades the liver, no medical or surgical treatment is usually possible. (It is not unknown to find a very early carcinoma in a gall-bladder removed for gall-stones, and then complete cure may result.)

Carcinoma of the bile ducts is very unusual, but carcinoma at the ampulla of Vater (whether primary at the end of the common bile duct or in the head of the pancreas does not matter clinically) is exceedingly common; it is, in fact, the most likely cause of painless obstructive jaundice arising after middle age. It must be noted, however, that gall-stones and carcinoma are not unlike in their age incidence, and gall-stones may be present and cause complete obstructive jaundice even although the patient has never suffered from biliary colic and pain. In all doubtful cases, therefore, an exploratory laparotomy is to be recommended. Carcinoma involving the head of the pancreas has hitherto presented an almost impossible problem for the surgeon, but a few successes have recently been obtained. Even when radical surgery is out of the question, one important palliative measure must never be forgotten. It is often possible, if the gall-bladder is not diseased or deformed, to join the fundus of the gall-bladder to the duodenum, thus providing free biliary drainage into the intestine and relieving the patient of all the misery of a persistent obstructive jaundice. The writer has had patients who have been able to continue work and enjoy fair health for almost three years after this palliative operation has been performed.

## APPENDIX

### INTRAVENOUS ADMINISTRATION OF GLUCOSE

Glucose is used for intravenous injection as a 5 per cent. solution in normal saline, carefully filtered and sterilized. It is often desirable, however, in order to reduce the bulk of the injected fluid, to give glucose intravenously as a 20 per cent. solution in normal saline. There is no danger in this, provided the injection is given slowly.

### GLUCOSE LEMONADE

$\frac{1}{2}$  lb. powdered glucose or 1 lb. commercial glucose.

1 quart of water.

Thin rind of two lemons.

Add glucose to water and lemon rind; boil for five minutes, strain, and when cold add juice of two lemons.

## DISEASES OF THE PANCREAS

Diseases affecting the pancreas give rise to very anomalous clinical and clinico-pathological disturbances. In health the pancreas performs two entirely independent functions.

1. The production of insulin by the islets of Langerhans—internal secretion.
2. The production of pancreatic juice—external secretion.

Disturbances of the internal secretion are discussed in the section on Diabetes Mellitus (p. 343) and only those affecting the external secretion, which are few in number, are discussed here. In some of them glycosuria may be coincidental but is rarely severe; if treatment is required it is the same as in diabetes mellitus.

Defects or deficiencies in pancreatic digestion may occur when the pancreatic juice is prevented from reaching the intestine, and from causes which inhibit the secretion or destroy the secreting cells. We do not know whether hypersecretion of pancreatic juice ever occurs, and the physician is only called upon to deal with the deficiencies. Moreover, it is only chronic deficiency with which we are concerned, since acute diseases, and especially acute hæmorrhagic pancreatitis, are entirely surgical in their treatment. Two chronic diseases—cyst of the pancreas and pancreatic stone—can also be dealt with effectively only by operation.

The diagnosis of chronic pancreatic disease is notoriously difficult and unsatisfactory. Its existence may be suspected when the stools are bulky, pale and frothy, and when the fat content is found to be high—60 to 80 per cent. instead of the normal 15 to 20 per cent. It must be remembered, however, that there are other causes of steatorrhœa, and also that when obstructive jaundice (due to many causes) is present fats may remain undigested from the absence of bile-salts rather than from any deficiency of pancreatic secretion. In carcinoma of the head of the pancreas—one of the commonest causes of obstructive jaundice in adults beyond middle age—both the biliary secretion and pancreatic secretion may be deficient in the bowel.

When chronic pancreatic disease has been diagnosed, treatment is carried out in two ways:—

1. A diet is prescribed low in fat but containing an adequate amount of carbohydrate and proteins. In severe cases predigested milk proteins can be given in the form of peptonized milk or Benger's Food.
2. An attempt is made to make good the deficiency of pancreatic juice by substitution therapy.

Substitution therapy has very slowly reached a useful stage of development. Pancreatic juice given by the mouth is valueless, since the enzymes are destroyed in the stomach. All remedies must therefore pass through the stomach unchanged, and several of these containing pancreatic enzymes are now available. Festan (Bayer) is prescribed as tablets (1 tablet or pellet three times daily, with, or immediately after, meals, swallowed without chewing) covered with a protective coating resistant to acid and only soluble



on reaching the intestine. It contains all three pancreatic enzymes. Panacoids (Reed and Carnrick) is prescribed as tablets "enteric coated," and each contains 2 gr. (0.12 gm.) of desiccated pancreas and 2 gr. (0.12 gm.) of desiccated duodenal substance. Dose, 1 tablet with, or just after, meals. Panteric tablets (Parke, Davis) are enteric-coated tablets containing the equivalent of 15 gr. (0.9 gm.) pancreatin (B.P.).

Pancreatic deficiency is so often only part of the picture of a disease that the physician must at the same time take full stock of other conditions affecting especially the liver, gall-bladder, stomach and duodenum.

## DISEASES OF THE PERITONEUM

There are few diseases of the peritoneum which concern the physician in the first place, except tuberculous peritonitis and ascites, both of which are dealt with elsewhere (see p. 154).

Localized chronic peritonitis or peritoneal adhesions may result from any intra-abdominal operation, no matter how carefully the gut is handled. At times no cause for adhesions can be found. Any subsequent operation merely adds to the number and extent of adhesions, and should never be done after the condition is recognized, except for definite obstruction. The sufferers from abdominal adhesions frequently lapse into a state of chronic invalidism, never being well but never seriously ill, and complaining of many and diverse symptoms of discomfort. The motor and other functions of the intestine are undoubtedly disturbed, but it is not to be wondered at that the symptoms become exaggerated after a time. No cure is possible but much symptomatic treatment, both physical and psychological, is required. Sedatives should be used with caution, and those of habit-forming type, especially opium, avoided. If a sedative is essential, it is best given in a mixture, the prescription not being shown to the patient. So far as physical symptoms are concerned, constipation and spasm of different parts of the bowel chiefly require treatment. Emuls. Paraff. Liq. Alk. (B.P.C.) is particularly valuable for the former, and 5 to 30 minims (0.3 to 1.8 c.c.) of tincture of belladonna is our mainstay for the latter.

J. W. McNEE.

# DISEASES OF THE HEART AND CIRCULATION

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## PRINCIPLES AND LIMITATIONS OF CARDIAC THERAPEUTICS

**T**HE axiom that the first stage in rational therapeutics is accurate diagnosis applies with particular emphasis in diseases of the heart and circulation. Just as a complete and exact diagnosis may safeguard the patient from unnecessary restrictions and ill-chosen remedies, so it must be realized that, with few exceptions, complete restoration of function is not to be anticipated, even with the most energetic measures at our command. Certain defects, by their very nature, are no material handicap and call for no treatment, while for others it must be admitted that remedies, however desirable, are unfortunately unavailing. There is no more important factor in determining appropriate treatment than the ability accurately to assess the degree of circulatory incapacity existing at the moment. It is a well-known fact that many a patient may have definite myocardial or endocardial lesions with striking physical signs and yet be completely free of all symptoms during ordinary activity or even during sustained physical exertion. Of these patients it may be said that their functional capacity is good. They require no treatment for the heart itself, and indeed it is often a question if by any reference to the heart their attention should thus be directed to their circulation. At the other extreme there are those who suffer from all the signs of heart failure even at rest: their functional capacity is minimal, and for them every effort must be made to ease the cardiac burden and relieve their acute discomfort. The first step in treatment, therefore, is the assessment of the degree of circulatory impairment, and this is gauged by the ease with which one or more of the three major cardiac symptoms—pain, dyspnoea or congestion—is induced.

It is important to note that a physical sign in itself, particularly when regarded as the only manifestation of organic damage, seldom warrants active therapeutic measures. A systolic murmur, an irregular pulse, even an enlarged heart, while each demanding careful investigation before its nature can be accurately determined, are not in themselves to be regarded as indications for any particular treatment. It is well known that, in the past, many a patient with a perfectly sound heart has been rested unnecessarily for months at a time on account of an innocent systolic murmur, and all to no purpose. Such a patient was perhaps lucky if he did not receive digitalis in some form or another, though no one has claimed that digitalis has the power to abolish a valvular murmur. Indeed on the contrary, by increasing the force of contractility, or by prolonging diastole, a murmur is often rendered more obvious. Similarly the waxing and waning pulse of sinus arrhythmia has given rise to difficulty. Here again digitalis, by increasing vagal tone, renders the arrhythmia more striking. This arrhythmia is not a manifestation of disease. An enlarged heart is com-

monly found in the athlete. As such it demands no treatment. On the other hand, the detection of an early diastolic aortic murmur during the course of a routine examination in a young or middle-aged adult may be the first sign to suggest a syphilitic aortitis, and thus provide a clue for the early treatment and prevention of future incapacity. There are exceptions to every rule, but it is a good principle which applies with particular emphasis in the therapeutics of heart disease to treat the patient when his symptoms warrant attention, and not his physical signs.

As a further principle it is reasonable to suppose that successful and appropriate treatment depends upon the removal or correction of the provoking cause of the cardiac distress. It has to be admitted, however, that while the ætiological cause of heart disease is often obvious enough, yet unfortunately it is but seldom that treatment can be regarded as successful in eradicating it. We know little about the cause of rheumatic infection, and can do little to eradicate, cure or prevent this important cause of heart disease. Hypertension is often apparently familial in its distribution. With a greater proportion of the population surviving to the later age-groups, it is only to be expected that hypertension and arteriosclerosis should play an increasingly important part in the production of myocardial damage, and all the more regrettable that in the present state of our knowledge we are unable to prevent the ultimate development of grave cardiac and circulatory symptoms by the eradication of the provoking cause. On the other hand, there is every reason for the belief that the rôle of syphilis in the production of heart disease is steadily decreasing, and, when recognized as an ætiological factor, cautious and appropriate treatment may be undertaken with ample justification. Similarly, in that group of cases in which over-activity of the thyroid plays a part, highly skilled surgical measures, appropriately undertaken, may lead ultimately to remarkable recoveries, if not, indeed, complete restoration of cardiac function. Thus it is that in many of the most chronic forms of cardiac disease we are handicapped greatly in the satisfactory treatment of the ætiological factors. On the other hand, there are those cardiac affections secondary to, it may be, acute fevers, anæmia, nutritional disturbances, chronic alcoholism, or digestive and dyspeptic conditions of one kind or another which may be greatly relieved by appropriate treatment of the exciting cause. In middle life the correction of obesity by dietetic means is of prime importance.

In the relief and treatment of circulatory dysfunction, without doubt the provision of adequate rest and the regulation of exercise demand a fine discrimination. The amount of rest to be recommended depends on the circulatory capacity of the individual. In the mildest cases it is only necessary to caution against undue fatigue: actual restriction of activities is unnecessary, and, indeed, should be avoided. There is every reason to suppose that the heart muscle in such people is improved in its tone by appropriate exercise. Unnecessary restriction will only lead to chronic invalidism, and often the production of an anxiety state regarding the integrity of the heart muscle. Much harm can be done by even the best intentions. For those who have dyspnoea or pain more readily induced on slight exertion, then a more sedentary and guarded life should be advised. They should be instructed to live well within their capacity so that symptoms are kept in abeyance. When distress comes more easily and symptoms begin to appear on slight exertion, then further periods of

rest and restricted activities are all the more desirable. Such people benefit from long hours of sleep, perhaps a minimum of nine hours, and many benefit greatly by a short rest after their midday meal. If for economic reasons that is not possible, then perhaps one day in bed each week may suffice to restore the circulation and enable the milder forms of exercise to be undertaken daily without real distress. If early signs of congestive heart failure be present, then more complete rest is urgently required, and a period of days or weeks in bed may be necessary.

The amount and degree of rest obtained by lying in bed varies a good deal from individual to individual: it is seldom sufficient merely to order a period of rest in bed without implicit instructions as to the procedure to be adopted. In the more serious cases rest in bed must be absolute, which implies, in addition to the most comfortable and restful position possible for the individual, that arrangements must be made so that he does nothing for himself. He is to be carefully nursed, lifted and helped into different positions as occasion demands: he is to be fed: he is to be denied all but a few visitors. Too often visitors are a tax on the cardiac patient, who is unfit to cope with the presence of even his closest friends. In no system of the body are the beneficial effects of rest as a therapeutic measure better exemplified than in the case of the heart and circulation. It is not an uncommon finding that even in cases of congestive heart failure adequate rest, a suitable diet, and appropriate nursing care may restore the circulatory capacity to reasonable proportions without the use of cardiac drugs. Such is the importance of rest and activity that each must be gauged in suitable amounts for each individual patient incapacitated by circulatory disease.

Recognizing the remarkable recuperative powers of the circulatory system, it is right to emphasize as a further principle of cardiac therapeutics that the patient must be supported in his illness by an uplifting and encouraging outlook. His progress at first is often slow, and, to allay his fears, ease his suffering and promote peace of mind, the doctor must bring with him to the sickroom a confident and cheerful atmosphere. Heart disease brings with it doubts and fears peculiarly its own, and these can best be countered by a clear statement of facts, tempered with that amount of judicious optimism which the experienced physician will find appropriate for the particular individual's emotional state and mental outlook. The stresses and strains of modern life, the anxieties and doubts which torment the mind of the sick person, throw a burden indirectly on the circulatory system. The doctor in his visit must try to shelter his patient from all the worries attendant upon his illness. A sympathetic understanding of these factors can do much to tide the patient onwards towards recovery.

As a further principle it is desirable to have clearly in mind the indications for the use of those drugs and mechanical procedures commonly employed in cardiac therapeutics. Pharmacopœial and proprietary preparations abound, but effective remedies are few. The discriminating physician will so restrict his therapeutic resources as to be thoroughly familiar with reliable and potent preparations of undisputed activity. The haphazard and indiscriminate use of drugs is at all times to be deprecated, but never more so than in the treatment of circulatory disease in which, with the appropriate use of potent preparations, so much of benefit can be readily accomplished. The intelligent use, for instance, of *digitalis* may be regarded as

one of the triumphs of modern therapeutics, and yet it is probably correct to say that more people suffer from lack of it than are ever poisoned by overdosage. Similarly the use of reliable hypnotics is of prime importance. Long and refreshing hours of sleep demand the use of well-chosen drugs, which can themselves appreciably shorten the time spent in confinement to bed. Symptoms such as cough, pain or excessive dyspnoea require appropriate treatment to ease the patient's burden. Each step taken is designed to lessen the work demanded of the heart, and by such means much can be accomplished. Dietary regulation has a similar purpose by the reduction of body-weight and the provision of an adequate supply of vitamins. The restriction of the protein intake, diminishing the specific dynamic action of the protein stimulus to metabolism, serves a similar purpose.

With these broad principles in mind it is desirable to reflect on the limitations of active therapeutic measures. At the outset it will, of course, be realized that complete restoration of function is seldom to be expected, and for the most part structural defects in the muscle, valves and arteries are permanent and irremediable. In consequence a limit is set to what may be attained even by the best régime possible. This must not be permitted to prejudice or discourage the doctor in his endeavour to give adequate symptomatic relief. The fact is that all the measures at our disposal can only alleviate cardiac failure in so far as the myocardium is able to avail itself of the proffered help. A time will surely arise when the futility of whipping the tired horse becomes more and more evident. Levine has pointed out that, for the most part, the best that can be accomplished by the intelligent care of chronic cardiac disease is a prolongation of life and relief from suffering, which compares very favourably with all the advantages that can be derived from the early diagnosis and modern treatment of malignant disease.

Few patients live to suffer from congestive heart failure on more than two or three occasions. By assessing the degree and duration of functional incapacity of the circulatory system one may often gauge roughly the extent of the improvement possible from the therapeutic measures to be employed. Fortunately many patients respond more satisfactorily than might be anticipated, provided every provision is made for thorough treatment and careful supervision throughout the illness. In this connection social and economic factors play an important part, for obviously the patient, safeguarded by a strong financial position, is more likely to reap the benefit of a prolonged rest and change than the labourer whose earning capacity is endangered by many weeks or months of strict medical care, and who in his younger years had no guidance regarding the selection of a suitable occupation in relation to the early cardiac damage. In the particular circumstances the physician must choose a middle course, adapting treatment to the peculiar personal conditions as best he may, and doing all he can to prevent the onset of more serious complications. The skilful use of the procedures of known benefit combined with the full co-operation of the patient, both in an economic and personal sense, will do much to ward off the fatal issue, ease suffering and prolong life.

It is gratifying to record that the intensive study of heart disease during the past twenty-five years has been rewarded by a great advance in its therapeutics, thus replacing the blind polypharmacy and inadequate care

of the past. Further gains will be made when the ætiological factors responsible for the ultimate development of myocardial damage can be prevented and adequately treated. Recognizing the limitations and encouraged by the possibility of aiding and guiding the recuperative powers of nature, it is with such broad principles as these that the physician approaches the treatment of heart disease.

A. RAE GILCHRIST.

## THE HEART AND CIRCULATION IN INFECTIONS

### RHEUMATIC CARDITIS AND RHEUMATIC FEVER

At the outset it should be stated clearly that treatment of this common and disabling condition is most unsatisfactory. The continued stream of adult cardiac cripples attending our hospitals, the subjects of valvular disease resulting from rheumatic infection in childhood or adolescence, is evidence enough that our treatment of the primary infection is not effective in preventing eventual cardiac damage. Figures such as those of Findlay make melancholy reading. He found that of nearly 700 cases of rheumatic infection in childhood, only one-third escaped cardiac damage, while one-third died within ten years of the first infection, and the remaining third became cardiac cripples, to die in early adult life. If such is the outlook for cases treated with all the resources of a modern hospital, it is apparent that the efficacy of our methods leaves much to be desired. The value of sulphonamide drugs in prevention of relapses appears promising, and their use may modify in future the gloomy prognosis of the past. Realization of the limitations of our therapy, however, must not discourage us from treating the victims of this disease as carefully and as intelligently as possible. Further, in the management of cases of rheumatic fever we must always bear in mind that in addition to the real victims of carditis, a large number of individuals without valvular lesions masquerade through life as cardiac cripples on the twin bases of an attack of rheumatic fever and a doctor's wrong assessment of a functional murmur (see also p. 608).

The two procedures which command universal approval in the management of rheumatic carditis and fever are rest in bed and the administration of salicylate. Contrary to expectations, both sulphonamides and penicillin appear to be useless in the treatment of this condition in the acute stage, though there are encouraging reports of the value of sulphonamides in prevention of relapses.

**Rest.**—The child who develops acute or subacute rheumatism should be confined to bed for a prolonged period, during which time he should be at complete rest. Good nursing is essential, and during the presence of active carditis the patient should not be expected or allowed to do anything for himself. The achievement of such complete physical rest in young children who have passed the stage of acute symptoms may present considerable difficulty, but confinement to bed should be maintained even although the child is moving about freely in bed, for to allow such a child up would at once increase greatly the demands made on the heart and circulation. During the period of fever, with its accompanying profuse perspiration, it is usual to keep the patient between blankets, thereby promoting absorption. Careful attention to the toilet of the skin is always necessary and will lessen

the risk of sudaminal rashes. The diet during this period should be fluid and light, as for any other febrile condition. The duration of bed rest is discussed below.

**Salicylates.**—By general consent, salicylate is regarded as without action on the progress of the cardiac lesions in rheumatism, but exerts a striking and specific effect on the other clinical manifestations, fever and arthritis. Despite misgivings expressed by some authorities, it appears to be without deleterious effect on the heart muscle, and its use, therefore, is not only permissible but imperative in cases with joint involvement. To withhold a remedy that relieves distress so strikingly is to be needlessly cruel; but it should be remembered that it masks the underlying active rheumatic process, and may mislead the unwary into a sense of false security.

To be effective the drug must be given in doses sufficient to produce the symptoms of mild salicylate intoxication: many so-called resistant cases are really due to underdosage. The actual daily dose required to produce saturation with the drug will vary naturally with the age and weight of the patient. The guide to the dose in any individual case is clinical: the abolition of joint pains and of pyrexia, or the development of mild symptoms of salicism (deafness, tinnitus, etc.). In general, for an adult, doses of 20 to 30 gr. (1.2 to 1.8 gm.) two or three hourly will be required, a total of 200 gr. (12 gm.) per day being commonly sufficient. In children the effective daily dose varies from 60 to 120 gr. (3.6 to 7.2 gm.) per day, according to age. Such doses may produce gastric irritation, and this may be the limiting factor in dosage. Sodium bicarbonate is usually given with the salicylate in doses of 20 to 30 gr. (1.2 to 1.8 gm.) for each 20 gr. (1.2 gm.) of sodium salicylate. This is generally accepted as a measure which reduces the risk of toxic manifestations, though the mode of action is debatable. In cases where sodium salicylate is badly tolerated, acetyl-salicylic acid may be substituted. Dosage again has to be pushed so far as the tolerance of the patient permits, or until gastric symptoms prove a bar to further increase. The soluble calcium salicylate, in doses of 15 gr. (0.9 gm.), may be substituted. Though freely soluble, this should not be prescribed in a mixture but in powder form, with instructions to dissolve one powder in cold water immediately before use. The intravenous administration of salicylate, formerly advocated by some and recently revived, has not been demonstrated to possess appreciable advantages over oral administration and the risk of toxic reactions is much increased.

The duration of salicylate therapy, on the scale of dosage advocated above, is short. Once the fever and pain have subsided, or when symptoms of salicism have appeared, the dosage should be reduced. This can generally be done within a few days at most from the start of treatment. The drug should not, however, be entirely discontinued, but should be administered in smaller doses so long as the rheumatic process is judged to remain active. The maintenance dose is that which will just suffice to keep pain and fever in abeyance, and for an adult is generally from 100 to 120 gr. (6 to 7.2 gm.) per day. Recurrence of acute symptoms is common when the maintenance dose is reduced as low as 60 gr. (3.6 gm.) per day. Should such recurrence occur, the dose must be temporarily increased.

**Local Treatment** for the affected joints should be simple. Wrapping the affected parts in cotton-wool and bandaging to secure rest generally suffice during the few days of acute pain. The application of a liniment of methyl

salicylate (B.P.) is in general use, but is of minor importance. Care is essential in those cases where pain lasts more than a very few days, for contrary to general teaching, permanent joint affection may result from rheumatic fever. This rare complication, practically unknown in young children, is seen now and then in adolescent patients. One has seen, for example, a case of acute rheumatic pericarditis in a young adult, with subcutaneous nodules, in which the affected joints included the temporomandibular and the small joints of the hands, and where lasting deformity was a sequel. The differentiation of rheumatic fever from "subacute rheumatoid arthritis" in such cases is highly artificial.

In cases where permanent joint changes follow, continuous immobilization during the acute stage leads later to limitation of movement, or even to fibrous ankylosis. It should be a rule, therefore, that passive movement through the maximum range, short of causing pain, should be performed daily so soon as the most acute symptoms subside, and immobilization during the rest of the day should be in a position optimum for function should fixation occur in spite of attempts to prevent it.

**Focal Sepsis.**—In many cases of rheumatic fever a focus of streptococcal infection in tonsils or upper respiratory tract remains active throughout the course of the disease. Considerable judgment must be exercised in deciding for or against radical treatment (*e.g.*, tonsillectomy) in such cases, since on the one hand a severe progressive or fatal carditis may follow an ill-advised operation, and on the other hand continued absorption from a heavily infected focus may be responsible for prolonged smouldering activity of rheumatic lesions. Operative interference is in general better avoided during the acute stages of the illness, though gargles, sprays and throat paints have a limited usefulness. When, after due consideration of the relative risks involved in radical and conservative treatment, a decision is made to remove infected tonsils or teeth, the operation should be preceded and followed by a few days' treatment with sulphonamide and penicillin. These are given in full doses, with the object of inhibiting the growth of organisms released into the blood stream from the focus at operation (see p. 71). The same precautions should be exercised before operations of similar type on apparently quiescent rheumatic cases.

It is convenient to discuss here the advisability of tonsillectomy in rheumatic children who are in a quiescent state. It appears that routine tonsillectomy of healthy children does not protect them against subsequent first attacks of rheumatic fever, and routine tonsillectomy after a first attack does not appreciably lessen the risk of recurrence of the rheumatism. It is probably wise to advise tonsillectomy only when the local condition is such as would demand operation in a non-rheumatic case, and then to choose the time for operation with great care.

**Duration of Rest.**—The question of how long a patient with rheumatic carditis is to be kept in bed is not easily answered. No hard-and-fast time limit can be laid down, though many clinicians advocate a minimum of three months rest in bed after even a mild attack. In previous editions of this book the writer stressed the distressing frequency with which one encountered patients with established valvular disease who related a history of arthritis treated by a short period of rest followed by a relatively quick return to normal activity. The view was expressed that it was wiser to assume the heart had been affected by rheumatism in every case, till time



had proved one wrong. These views were founded on experience in the wards and out-patient departments of teaching hospitals, and on cases seen in consulting practice. To-day, after six years' army experience, one is compelled to modify one's opinions. In a very large proportion of men referred by medical officers as cases of valvular lesion there is in fact no such affection. In fully one-third of all cases with symptoms of the "Effort Syndrome" group admitted to a special centre for rehabilitation, the onset of the symptoms and of the disability could be traced to a doctor's warning to parents or patient that all forms of strenuous activity must be avoided. It is true that in all cases with clinical evidence of *active* carditis, rest in bed should be prolonged so long as the signs of activity persist, and this may extend over a period of many months. It is a culpable error, however, to prolong rest after signs of activity have disappeared. Not only is an established though quiescent valvular lesion not benefited by such treatment, but there is evidence that moderate exercise is beneficial for the subjects of early valvular disease.

The criteria for determining quiescence of the endocardial inflammation must therefore be considered. It must be realized that a smouldering inflammation may go on in a valve for many months, and that a process of sufficient intensity to produce eventual gross fibrosis may exist with very little clinical upset. Pulse-rate and temperature may be normal and gross cardiac enlargement absent in the presence of active valvular mischief. Sinus arrhythmia is no longer regarded as a safe indication that the heart has escaped damage, and we have repeatedly confirmed Parkinson's observation that active carditis and sinus arrhythmia may coexist. As is well known, the duration or degree of joint involvement bears no relation to the extent of the cardiac lesions. Subcutaneous nodules when present are indicative of activity, but their absence does not exclude active carditis. The return of the blood sedimentation rate (B.S.R.) to normal is probably as sure a guide as any to the cessation of activity. The B.S.R. is raised in all cases of active carditis, except those with gross congestive failure, but in these cases the failure is easily recognized, and the question of allowing the patient up does not arise. A raised B.S.R. naturally does not necessarily indicate carditis, for many conditions increase it, *e.g.*, tonsillar sepsis. By careful clinical examination the true significance of a raised B.S.R. can usually be assessed. Other criteria of cessation of activity are gain in weight in children (not due to oedema), stabilization of the position of the apex beat and of physical signs in the heart, and a stable pulse-rate, particularly that taken during sleep.

Children who have suffered from repeated attacks of carditis may develop a severe acute pan-carditis, which may progress to end fatally. The handling of such a case is as sad a task as any that a doctor has to face; we are devoid of measures to arrest or even retard the disease, and treatment, while never meddlesome, must be directed to relief of cardiac failure and of distress from dyspnoea, sickness, sleeplessness and pain.

**Convalescence.**—When the period of complete bed rest is over, the return to activity should be very gradual, and should be carefully supervised. Any suspicion of recrudescence of the rheumatic process should be met by a prompt return to complete rest as in the acute attack.

The child who has weathered a rheumatic carditis is frequently sent for a short period to a convalescent home, and then returns to school and to

full routine. This is not satisfactory, and is probably responsible for much disability in later life. Convalescence should be protracted, and after the period of hospital treatment the child should be sent for a residence of at least some months, but preferably for a prolonged period (six to eighteen months), to a convalescent home. In some parts of the country special homes have been established by local authorities for such convalescent rheumatic children, where adequate medical attention and supervision are available in healthy surroundings, much on the lines of sanatoria for tuberculosis. The early manifestations of recurrence can thus be recognized and timeous hospital treatment instituted. These homes are not designed for children already the subjects of advanced cardiac disease, for whom unfortunately little can be done, but for the large number of early or incipient cases of cardiac involvement in whom some abatement or arrest of the mischief may be looked for. Provision for the education of the children in such homes is essential.

There is unfortunately a very real danger that the individual who has been thus safeguarded to the best of our ability from a life-shortening organic disability, may become a burden to himself and the community from the development of a cardiac neurosis, to which such treatment may predispose.

**After-care.**—On discharge from such an institution, or after long convalescence at home in areas with no such facilities, the child should return gradually to activity, the limitation of effort being determined by the extent of the cardiac damage. In cases with mild but quiescent cardiac valvular lesions full activity is allowable, with a prohibition only on such strenuous exertions as competitive sports. Cases with gross damage and marked enlargement must, however, lead quiet, non-strenuous lives. Careful follow-up with periodic assessment of general health and cardiac condition is essential, and any suggestion of renewed rheumatic activity demands prompt measures of rest in bed, etc.

There is statistical evidence that the prophylactic use of sulphonamide or sulphathiazole in doses of 0.5 gm. daily during winter and summer for some years is of value in preventing exacerbations of the rheumatic process, despite the ineffectiveness of these drugs in acute established relapses. There is a slight risk of toxic side-effects, of which agranulocytosis is the most serious, but the low incidence of these compared with the known high death-rate from relapsing carditis justifies the use of the drugs.

The choice of a future occupation should always be made under the guidance of the doctor. Instances of children or young adults with advanced cardiac lesions engaged in strenuous occupations are all too familiar. Such cases would not occur if efficient after-care were carried out. In this connection it is well to emphasize that the education of a child should not be neglected during long periods of semi-invalidism. Many rheumatic children leave school at fourteen years with much less than average schooling and are driven on to the unskilled labour market. Better education means better ability to secure a sedentary occupation which will not lead so soon to a cardiac breakdown.

In this country there has been little organized attempt to secure appropriate employment for the adolescent cardiac cripple, though in America the problem is tackled on a nation-wide scale. There is ample scope for the doctor, in village or city, to make himself acquainted with local indus-

tries, and by direct approach to employers of labour to secure the right niche for an individual patient. Light, skilled crafts (wood- and leather-work; radio mechanics; precision instrument making and watchmaking, etc.) are remunerative, make little call on physical strength and maintain the patient's interest and independence.

It is implicit in these remarks that diagnosis must be accurate. Far too many children are lightly diagnosed as suffering from valvular disease on the basis of a systolic or exocardial murmur unaccompanied by cardiac enlargement, and it is fair to say that for one young adult with a mitral stenosis that has been missed by his doctor one sees ten cases with innocent murmurs labelled organic. When such important matters are involved as the whole future life of a young patient, his choice of vocation or her fitness for eventual marriage and childbearing, it is surely incumbent on the doctor to exercise the greatest care. As the diagnosis is admittedly often difficult, the doctor should seek whatever specialist and radiological help may be available to him before pronouncing an opinion. A thoughtless remark after a superficial examination is potent for evil.

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### NON-RHEUMATIC ENDOCARDITIS

**Subacute Bacterial Endocarditis.**—Until recently this disease was almost invariably fatal. Within the last three years the whole outlook has been revolutionized by the employment of penicillin in its treatment. The collective investigations sponsored by the Medical Research Council of Great Britain at various selected hospital centres have yielded results which have exceeded all expectations. The facts so far gathered suggest that a 95 per cent. mortality has been replaced by a 70 per cent. recovery rate—surely penicillin's most remarkable achievement.

In planning treatment it is desirable to recover the causal organism from the blood, commonly a streptococcus viridans—a normal inhabitant of the mouth—and have its degree of sensitivity to penicillin determined by the bacteriologist. The standard Oxford staphylococcus has a coefficient of resistance to penicillin of 1. Different strains of the streptococcus viridans vary in their resistance, but in general the coefficient of resistance is approximately equal to that of the standard staphylococcus. Exceptionally the coefficient of resistance to penicillin is high and, if over 16, heavier dosage and a more protracted course of treatment will be desirable. Should the organism be insensitive to penicillin, then streptomycin or some other antibiotic should be employed if the organism is found to be sensitive to it.

For the usual patient a total daily quantity of 500,000 units of penicillin continued for 28 consecutive days yields results unsurpassed by any other system of dosage. The drug is given by intramuscular injection at 4-hour intervals by day and night without interruption. When 500,000 units is the daily quantity it is convenient to employ 4 doses each of 100,000 units and 2 doses each of 50,000 in the 24 hours. Intramuscular doses by this scheme are less exhausting to the patient than might be supposed and are preferable to the continuous intramuscular drip, which is unsuited for the prolonged therapy necessary for success in this disease. The gluteal regions are selected and the injections made with the usual precautions at sites varying as widely as possible in order to reduce the local irritation of the

repeated needle pricks. On occasions the scapular muscles may be selected to rest the hips and thighs.

In successful treatment the length of the penicillin course is even more important than the daily quantity. The investigations made to date indicate that a 28-day course of treatment produces consistently better results than any other scheme so far devised. The shorter the course, the greater is the tendency to an early reactivation of the infection. Should the infecting organism be unusually insensitive to penicillin—*i.e.*, with a coefficient of resistance of 16 or more, heavier daily dosage and a more protracted course should be ordered. Similarly, should the patient relapse, with a recurrence of the organism in the blood and evidence of a reactivation of the lesion, a longer course of penicillin should be recommenced. The second course should not be less than six or eight weeks. There is evidence to suggest that a previous course of penicillin is prejudicial to the success of a further course unless the second course is greatly prolonged. For this reason, in the event of relapse, it is wise to prescribe a double course—56 consecutive days with a daily amount of 2,000,000 units, in place of the 28 days of the original course. It cannot be too strongly emphasized that there is no place for half-hearted measures in the treatment of this disease. Short courses, irregular hours of administration, and a dosage less than 500,000 units daily, invite relapse and thereby render ultimate success more difficult to attain and make recovery more protracted.

When relapse occurs, as it occasionally will even under the best régime, it is usually observed within four weeks of the completion of the course of treatment. It is therefore desirable to have the patient, despite his apparent well-being, under daily observation for at least a month after the cessation of penicillin therapy. It is remarkable to note the improvement in nutrition, the disappearance of anæmia, the subsidence of fever and the obvious gain in weight and strength which accompany recovery. Relapse is heralded by tachycardia, a climbing temperature, a failure to maintain weight and by the recovery of the organism from the blood.

When good progress is made from the start of treatment, relapse is unlikely, but it seems inevitable that perhaps 30 per cent. of sufferers will die of the disease as a result of such major complications as congestive heart failure, massive infarctions or uræmia. Good nursing, symptomatic remedies, a nutritious diet and a gradual convalescence are to be encouraged. As a general rule the patient is able to be up from bed and moving about quietly within a month of completing the penicillin course.

**Ulcerative (Acute Bacterial) Endocarditis.**—Similar measures to those recommended above are to be employed in this disease. The prognosis has been vastly improved by the use of penicillin in the dosage employed in the subacute variety, and already cures are being reported in what was once an almost invariably fatal condition.

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### PERICARDITIS

A patient suffering from acute pericarditis, whatever the ætiology, should be nursed at complete rest in bed. In the common variety occurring in the course of an acute rheumatic carditis, the general lines of treatment are as described under that heading. In tuberculous cases the general

measures are those appropriate to tuberculous cases in general. Cases which occur in association with pyogenic infections (hæmolytic streptococci, staphylococci, pneumococci, etc.) are treated along lines indicated by the infecting organism (see pp. 71, 86), the possibility of the development of a purulent effusion being kept in mind.

The relief of pain may call for treatment, though many cases suffer surprisingly little discomfort even in the presence of a gross friction rub. Mild analgesics such as sodium salicylate, or acetyl-salicylic acid, or codeine in doses of  $\frac{1}{4}$  gr. (16 mg.) may suffice, but severe pain may necessitate the administration of  $\frac{1}{4}$  gr. (16 mg.) of morphia hypodermically, with the customary proviso regarding its dangers in young children.

Counter irritation for the relief of pain has been employed for many years, usually by cantharides blisters. Should such be employed, the plaster should be applied in one or two small pieces the size of postage stamps, and large blisters to cover the precordium should never be used. The discomfort produced, the risk of septic skin infection or of toxic absorption from the area, and the interference with subsequent examination of the precordium all render such large blisters most inadvisable. The usual sites for application of small blisters are slightly to the left of the sternum near the base of the heart, or midway between apex and sternal margin. The cantharides is left in position for six to eight hours, or until a blister is raised. The plaster is then carefully removed, the blister snipped with scissors and loose skin removed, and the bare area dressed with an emollient and a sterile dressing held in place by adhesive tape. How far such treatment aids recovery is uncertain. Relief from pain can be more easily attained by simple prescription of analgesics, and, in the case of sensitive children at least, the method has obvious disadvantages which seem to outweigh the claimed benefits. The use of an ice-bag, on the other hand, may give considerable relief from pain without the discomforts attendant on blistering. The ice-bag should be only partially filled with finely chopped ice, to which salt may be added. The bag should be applied to the bare skin of the precordium, and is best suspended from some improvised form of cradle so that the weight of the bag may not cause oppression. It is well recognized from experience in auscultation that pressure over the ribs increases the pain in acute pericarditis.

The development of a large effusion may be associated with symptoms due to embarrassment of the heart's action or to interference with respiration due to partial collapse of the left lung. It is unusual for such symptoms to be severe enough to warrant aspiration of the pericardial effusion, but this rarely may have to be done where cyanosis and dyspnoea are extreme or where the pulse is so far reduced in volume as to be hardly perceptible. Aspiration should be done for diagnostic purposes where there is a question of pus formation in the sac, as in pericarditis developing after pneumonia, or in the course of a septicæmia after osteomyelitis, etc. In these cases the aspiration of a few cubic centimetres of fluid will suffice, while for relief of pressure effects the aspiration of several hundred cubic centimetres may be necessary. The technique of paracentesis is described on p. 947.

The discovery of pus in the pericardial sac is an indication for surgical intervention. Drainage may be established by open operation, with resection of ribs, or may be achieved by a closed method, by insertion of a tube into the sac through the soft tissue of an interspace and the main-

tenance of suction. Both methods yield good results, and the decision as to which to employ naturally lies with the surgeon operating.

In non-purulent cases recovery with absorption of the effusion is the rule, except in the cases of terminal acute pericarditis which occur in the last stages of Bright's disease and similar cachectic conditions. Convalescence may be slow, and there is no efficient method of hastening the absorption of the fluid. Repeated assessment of the size of the effusion and of the patient's general state will guide the physician in his decision as to management—when to allow the patient to move about in bed, when to allow him up, etc. The general principles for cases of rheumatic carditis are applicable to cases of pericarditis of similar ætiology. Other cases, on recovery from the acute attack, may be allowed fair liberty of exercise, etc., but should be re-examined from time to time during the ensuing years to exclude the development of other lesions or of chronic constrictive pericarditis.

Chronic constrictive pericarditis is a surgical problem, and is dealt with in the section on The Surgery of Cardiac Conditions (p. 670).

### CIRCULATORY FAILURE IN ACUTE INFECTIONS

In the circulatory failure which occurs in acute infections such as lobar pneumonia, two factors are at work: central, due to failure of the poisoned heart muscle, and peripheral, due to failure and dilatation of the poisoned small vessels. Of the two the peripheral failure is generally the more important. This is true even in diphtheria, where many of the deaths are due to peripheral failure, though in some cases the specific action of the toxin on the heart causes sudden (cardiac) death, often many days after the apparent subsidence of the maximum effects of the acute infection.

The treatment of toxæmic circulatory failure really lies in its prevention by early and adequate treatment of the underlying infective condition. In diphtheria, for example, the timely administration of potent antitoxin reduces greatly the incidence of cases with dangerous circulatory failure. So in pneumonia, early and efficient specific treatment with sulphadiazine and penicillin will lessen the risk of later intractable toxæmic effects. In diseases where no specific antiserum exists, or where failure develops during a long illness (*e.g.*, typhoid fever), general measures to reduce toxæmia are employed to the best of our ability.

Once failure has developed, the prospects of successful treatment are not good. It is by then too late for efficient specific therapy, and measures calculated to stimulate the heart or the periphery are disappointing. Of drugs which act on the heart, digitalis is the most widely employed. The use of digitalis in pneumonia, for example, is traditional, though its value is doubtful. It is claimed that in some way the drug improves the efficiency of the heart's action, though even its advocates admit that the heart-rate is not slowed. It is the impression of many clinicians that the use or omission of digitalis makes no difference to mortality rates in lobar pneumonia. This has been confirmed statistically by certain large-scale observations. The lack of demonstrable effect on mortality holds for cases who were fully digitalized. Cases who receive the drug for the first time near the day of the crisis, and in small doses, manifestly are never digitalized to an extent which would render probable any action on the heart.

Many other drugs which enjoy a reputation as cardiac stimulants, and

which are widely used in conditions of toxæmic circulatory failure, are devoid of direct action on the heart. Strychnine appears to act solely on the central nervous system, and the class of "diffusible stimulants" (sp. æther. nitros.; sp. ammon. aromat.) act reflexly through the same system. None of these is a true cardiac "tonic," increasing the efficiency of the muscle. Adrenaline, it is true, has such an action, but it increases the tachycardia which is already a disquieting feature of toxæmic failure, and is known to deplete the glycogen reserve of the heart muscle cells. In short, we do not possess any drug which can whip an exhausted heart to renewed activity, or which can render the cells immune to circulating toxins.

Peripheral vascular dilatation, as the principal element in the production of circulatory failure, more frequently demands treatment than the heart condition. Many drugs are available, adrenaline, pituitary extract, leptazol, nikethamide, intravenous hypertonic glucose, etc., and these are discussed in the section on Acute Circulatory Failure (p. 678). The results of their use in toxæmic states are by no means satisfactory. In fact, once such failure has developed, progression to a fatal issue is likely in spite of all therapy, unless the natural body processes succeed in overcoming the toxæmia, as in the crisis phenomenon of lobar pneumonia.

#### FOCAL SEPSIS IN RELATION TO HEART DISEASE

The exact rôle of focal septic infection in the production of heart disease and symptoms is somewhat uncertain. It is recognized that the *Streptococcus viridans* may gain access to the blood from foci, especially in the teeth, tonsils and upper respiratory tract, and may give rise to a subacute bacterial endocarditis in persons with damaged heart valves. For this reason it is advisable to search for, and extirpate, such foci in all cases of congenital heart disease and in the subjects of rheumatic lesions. Of these latter, it is the cases of aortic disease or early mitral disease who are liable to develop endocarditis lenta; late cases of mitral stenosis are rarely affected. The operation should be carried out after preliminary administration of protective doses of sulphonamides or penicillin.

It is also admitted that foci of sepsis may be of ætiological importance in cases with heart block of milder grades, and in cases with obstinate extrasystolic irregularities. In such cases also, removal of the foci is desirable and generally without risk if suitable prophylactic measures are taken by pre- and post-operative treatment with sulphonamides (see p. 71).

The matter is not so simple, however, when symptoms or signs of gall-bladder disease are found in a case presenting clinical evidence of heart disease. It is held by some that many cases of cardiac pain and of congestive failure may owe their condition to toxic absorption from an infected gall-bladder. Other clinicians contend that chance association plays a part in the simultaneous occurrence of the two conditions. The subjects of cholecystitis are of the habitus and age which favour arterial degeneration and its sequelæ of angina and myocardial failure. The evidence in favour of the so-called "gall-bladder heart" is thus not convincing, and operations for removal of the gall-bladder should only be undertaken when there are clear indications, apart from the cardiac condition, to justify the step. The high mortality which attends this operation in cases with hypertension, obesity and impaired myocardial efficiency should be kept in mind.

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## THE MANAGEMENT OF THE AMBULANT CARDIAC PATIENT

The energetic treatment of heart disease is chiefly concerned with measures to counteract the more advanced grades of the different types of heart failure, but it is no less important to learn the management of the minor degrees of incapacity in order that life may be rendered more tolerable, and serious failure avoided or postponed. The great majority of cardiac patients are able to go about, and, though their activities are restricted, yet with suitable guidance and advice from time to time they can generally lead useful lives of moderate activity. Their appropriate care and supervision depends upon a number of factors, of which the more important are the degree of circulatory impairment, the age of the patient, and the ætiological cause of the heart disease. The extent of the cardiac damage, the occupation, the environment, the economic circumstances, the habits and, to some extent, the man's personal character and mental outlook influence treatment in its widest sense. By this is included the individual's ability to conform to the rules of healthy living, and his willingness to co-operate in the details of therapy as advised by his physician.

It is recognized that, with few exceptions, myocardial damage is an irreversible process, and tends of itself to run a progressively downward course over the years, ultimately terminating in one or other type of heart failure, or the end may come suddenly as a result of an abrupt coronary occlusion or from some other vascular catastrophe such as embolism or rupture of a cardiac or aortic aneurysm. Briefly stated, the objects in treatment during the ambulant stage are to arrest or retard the downward course by decreasing the cardiac burden and so to improve the general health of the patient that the liability to infection is reduced. It may thus be said that the patient has to be taught the principles of healthy living and treated according to the severity of the circulatory handicap.

**Habits.**—It is always worth while to review briefly with the patient his habits of life, so that these may be adjusted to conform with physiological principles. Hours of work and hours of sleep are a first consideration. The general health of many people complaining of minor ills of one kind or another is improved by insisting on a minimum of eight hours' sleep each night, and for the great majority of cardiac patients this is certainly a minimum. Nine to ten hours is often preferable, and even though all this time may not be spent in actual sleep, the mere rest and relaxation is of very definite value, particularly if it become a regular habit. Hours of work vary enormously in different trades and occupations. Certainly in the minor degrees of cardiac embarrassment a maximum of eight hours is as much as most people can accomplish; if more is attempted, then suitable intervals of rest should be provided. Each individual requires special consideration, but there is no doubt that the avoidance of the rush and tumble of everyday life, and the substitution of regular habits and a quiet and moderate routine, with gentle outdoor exercise from day to day, promotes general well-being. Harm results from too sheltered a life. Muscular exercise up to the point of inducing a healthy degree of fatigue and restful sleep is by its invigorating character of value to the cardiac patient whose response to effort is not greatly impaired. Moderation in food, in drink and



in tobacco is to be encouraged. The avoidance of infection, particularly infection of the respiratory tract, is of prime importance to the cardiac patient. This is not always easy, but suitable clothing and an abundance of fresh air at all times, with adequate ventilation of the living-rooms at home and in the office and workshop, decrease the risk. In the winter months particularly, when exposed to cold and damp, and when respiratory infections often of minor degree are rife, the cardiac patient is wise to avoid hot, stuffy rooms, crowded places of entertainment and public meetings. Infections of the nose and throat—catarrh and, in particular, bronchitis—throw a considerable burden on the heart and circulation, and may in themselves be responsible in susceptible subjects for a decline in the cardiac reserve and the actual precipitation of congestive heart failure. It is therefore proper that when an infection becomes manifest, particular care should be taken, and the patient advised to keep to his bed until free of symptoms. Otherwise the cardiac patient must be encouraged to take such exercise as he can up to the limit of his tolerance, provided always that he is ensured a sound and restful sleep each night. His activities are only to be restricted to such a degree that symptoms are avoided. He can take exercise short of producing dyspnoea or undue fatigue.

**Exercise.**—The amount of exercise suitable for the individual can only be found by actual experiment. Activities are only to be limited when they are sufficient to induce symptoms, undue fatigue, dyspnoea or pain. Thus it is that the degree of circulatory impairment is gauged by a study of the patient's reactions to exercise. The less readily these are induced, the less restriction of activity is required. By living up to the capacity of his tolerance for exercise the more likely is his range of activity to increase. Fatigue or breathlessness decides that his tolerance has been approached or passed, and the rate and amount of work in the future must be reduced to conform with his endurance. Similarly, pain is a signal that the work done has been in excess of that with which the blood supply of the myocardium can cope. Simple restrictions designed so to limit activity that symptoms are kept in abeyance are all that is required in the first instance. Golf, tennis, riding, swimming and even hill walks are permissible, and should be encouraged. Improved tone of the skeletal muscles is associated with an increased capacity for cardiac work. The latitude permitted varies with each individual and the ease with which his physical condition improves.

A further degree of incapacity becomes evident when ordinary activities of a mild nature, such as quiet housework or simple walks on the level, are sufficient to induce fatigue, dyspnoea or discomfort. Social and business activities must be restricted to a greater or less extent. This degree of disability is frequently associated with minor degrees of peripheral oedema noticed about the ankles towards evening. This is a sign of great significance and indicates that more active measures are required if congestive failure is to be avoided. In the mildest cases a few days' rest in bed, with or without the use of digitalis, and the provision of ample sleep are measures designed to restore a more satisfactory blood flow. A week or ten days in bed will often enable the circulatory incapacity to right itself, and, thereafter, when activities of a mild degree are resumed, it will usually be necessary to insist on at least one day in bed each week, a rest of an hour or two after the midday meal, and the regular addition of an extra hour in bed each night for some months. Digitalis may be given in small doses of 1 to 2 gr.

(0.06 to 0.12 gm.) of the powdered leaf thrice daily, generally for a week or ten days at a time with three or four days of freedom from the drug.

**Focal Sepsis.**—In the supervision of the patient in the ambulant stages of heart disease, it is always advisable to have local sepsis, particularly in the mouth and throat, eradicated. The teeth should be overhauled at regular intervals by a competent dentist, the tonsils dealt with if any evidence of local sepsis exists, and appropriate treatment should be undertaken for sinus infection. By removing and correcting infection in these situations much can be done to reduce the tendency to minor respiratory ills, catarrh and infection of the respiratory tract.

**Anæmia.**—Similarly it is always wise to be on the lookout for even minor degrees of anæmia. Many cardiac patients, especially women, convalescent from rheumatic infection may remain mildly anæmic for months or years after the original infection has died out. Their cardiac symptoms are aggravated by a diminished hæmoglobin content. Their general health can be improved and their fatigue and dyspnoea lessened when the anæmia is completely corrected by adequate doses of iron for such periods as are necessary. For this purpose ferrous sulphate in doses of 3 gr. (0.18 gm.) three times a day may bring about a striking amelioration of symptoms, particularly with regard to fatigue, and sometimes with relief of pain and præcordial discomfort. Such minor measures as these will do much to maintain the cardiac patient's general health and improve his response to effort, but if with the passage of time a further stage of decompensation is reached and the tendency to congestive failure, nocturnal dyspnoea or anginal discomfort increases, then longer periods of rest are obviously required. The active therapeutic measures for these different types of heart failure are fully discussed on p. 631 *et seq.* In convalescence, after failure has been adequately corrected, drug treatment is almost invariably required, and must be supervised thoroughly from week to week. Digitalis in maintenance doses (p. 642) should be prescribed up to the limit of tolerance when it is indicated, physical activities greatly limited and sound sleep ensured.

**Age and Occupation.**—The age of the patient is of some importance in determining suitable treatment. In infancy, for instance, the severer grades of congenital heart disease necessitate advice regarding feeding and nursing (p. 628). In childhood and adolescence rheumatic heart disease is prevalent. The rheumatic child, when the active infection has subsided, requires much the same after-care as the tuberculous patient. In this way prolonged semi-convalescent treatment in an institution where the child's education may be continued without the rough and tumble of school life has much to recommend it. In this country the demand for accommodation of this nature is increasing, and various residential homes are available where, under prolonged supervision, with adequate control of the diet, rest, exercise and lessons better progress can be made than in the environment in which the rheumatic infection was originally acquired. Not many of these residential homes are available to the child of middle or better class parents. Where economic circumstances permit, it is justifiable to recommend that these children be taken abroad to tropical or sub-tropical countries where the likelihood of reinfection is diminished, and where, with exposure to sunlight and adequate feeding, nutrition is improved. For this reason the Mediterranean coast, the Canaries and Egypt are often selected for a prolonged convalescence of six or twelve months. Treatment at this stage is

directed more to the prevention of infection or its reactivation than to the actual cardiac disease. When the child is ambulant and sufficiently advanced in convalescence to resume even modified school life, continuation of particular care is required so that under-nutrition is prevented, excessive fatigue avoided and exposure to cold and damp minimized, all of which are known to lower resistance and favour reactivation of the carditis. It has already been pointed out that every attempt should be made to educate the rheumatic child so that in later life he may earn his living in a sedentary occupation. In caring for these children the doctor should be prepared to advise the parents regarding the child's employment. In this country an outdoor occupation is inadvisable. Work involving physical strain and sudden or sustained muscular effort is likely to prove detrimental. Employment at a bench, desk or counter is usually preferable. Clerks, book-keepers, typists, telephone operators, cashiers, dressmakers, tailors, all hold sedentary jobs suitable for the young cardiac patient. Similarly there are such skilled trades as electrical mechanics, radio repairers, watch, fountain-pen and jewellery makers to which the youthful rheumatic patient may be suitably apprenticed. Too often it is the journey to or from work which taxes the strength. Greater consideration for the occupational training and employment of the cardiac cripple in suitable industries will be rewarded by happier and longer days for these patients.

In middle age, heart disease curbs a man's activities, and when symptoms begin to interfere with the daily routine, a definite modification of his habits and methods of living must be prescribed. Few people are quite so indispensable in their work as is often imagined, and deputies can often be found to share the responsibilities and ease the burden. It depends on circumstances whether restriction should be applied first to the daily occupation or to the hobbies and philanthropic activities. Too many men are allowed to retire from active work without sufficient interests to occupy their minds. The business man in early middle life handicapped by organic heart disease must of necessity be advised to limit his ambitions, lead the quieter life, have longer holidays and rely more and more on his staff for all routine work. At this age period the commoner ætiological factors are hypertensive and syphilitic heart disease, the latter less common than formerly.

### ESSENTIAL HYPERTENSION

Elevation of the diastolic blood pressure in consequence of increased arteriolar-tonus is no more a disease entity than a rise of temperature or a sustained tachycardia. While it is to be regarded as a physical sign common to a number of diseases, hypertension if long maintained is itself productive of widespread degenerative vascular changes. Its malevolent influences on the retinal, renal, cerebral or coronary systems profoundly influence the welfare of the individual. As a leading cause of death and with peculiar complications more devastating than those of malignant disease, hypertension remains a therapeutic problem, the successful solution of which would change the whole complexion of medical care and supervision in the middle-aged and in more elderly age groups of the population.

Despite the brilliant and painstaking efforts of many investigators during recent years, no specific remedy is yet available. Treatment falls short of the ideal, and yet by symptomatic and palliative means much can

be done to ease the situation and make life more tolerable for the sufferer. On account of our almost invariable inability to eradicate the root cause or to repair the damage done to the vascular tree, it is perhaps all the more important to bear in mind simple principles in the treatment of these hypertensive people.

**Principles of Treatment.**—The first principle is to make sure, by repeated readings of blood pressure under varying conditions, that hypertension in a pathological sense does in fact exist. A solitary reading in a patient unfamiliar with the technique of blood-pressure determination in unaccustomed surroundings, apprehensive and ill at ease, is valueless and only confusing. A minimum of twenty minutes' rest on a couch should be allowed, the patient comfortably reclining, before the lowest of a succession of readings is accepted as abnormal. A diastolic pressure of 95 to 100 millimetres is outside the accepted standards of normality at any age, provided always that successive readings establish its consistent elevation.

As a further step, it is the doctor's duty to clarify his diagnosis. By careful history-taking and close attention to the details of physical examination, aided on occasions by special technical investigations, it is commonly possible to discover a clue as to the disease entity underlying the production of the elevated pressure. This is not the place to discuss questions of differential diagnosis, but it is worth while to recall that hypertension may be secondary to some well-established entity such as coarctation of the aorta, polycystic renal disease, chronic glomerular nephritis or Cushing's syndrome, to mention certain possibilities. A second group of cases is composed of those in whom there exists some local lesion of the urinary tract potentially remediable in nature. A unilateral pyelonephritis in a young subject, or, as a further example, the impediment to urinary outflow arising from prostatic obstruction in an elderly man, are both instances in which an alleged remediable cause, or at least an aggravating factor in the production and maintenance of the hypertension, may be susceptible to appropriate treatment. When hypertension is due to a unilateral renal lesion, early diagnosis is of the utmost importance as damage to the contralateral kidney, the result of continued hypertension, militates against any therapeutic success. Nephrectomy under such conditions is practically confined to children.

Although the above examples are recognized causes or accompaniments of hypertension, yet the great majority of cases coming before the physician fall into neither of these two groups. When no cause can be discovered, and in particular when there exists no inflammatory or obstructive renal lesion, the diagnosis of essential hypertension thus reached by a process of elimination is made with more confidence. For the majority of sufferers no specific remedy exists, a rational therapy remains undetermined, and treatment, be it medical or surgical, is symptomatic and palliative.

Having established the diagnosis, it is a sound principle at the outset of treatment to reassure the patient. By his manner, attitude and general demeanour, supplemented by a simple statement of fact, the doctor can do much to allay anxiety. The appropriate amount of encouragement and reassurance depends to a large extent on the physician's assessment of his patient's emotional outlook, knowledge and understanding of his complaint. As a general rule the fears of high blood pressure should be countered at the earliest opportunity, with the explanation that the condition is known to

exist for many years and may even subside spontaneously without either serious embarrassment or permanent crippling. There is no doubt that the great majority of sufferers respond in some measure to conscious or unconscious psychological treatment of this nature. They feel better and make more headway when under the protective and understanding care of a sympathetic but enthusiastic adviser. Relief from emotional tension is therefore an important therapeutic step, and the doctor should establish confidence and banish anxiety at his first contact with his patient. Only exceptionally is it necessary with over-confident people to emphasize the dangers or to issue a warning.

As a further principle the doctor must be on his guard lest he hastily attribute either symptomatic relief or a fall of pressure to the particular remedy in use. Though associated usually with a progressive structural disorder of the arteriolar system, hypertension commonly runs a prolonged course over the years and shows of itself many periodic fluctuations in intensity, frequently interspersed in the most unpredictable way by spontaneous improvement in symptoms and often by a temporary decline in blood pressure to surprisingly low levels. These natural remissions make reliable therapeutic deductions all the more difficult. For the same reason there is little to be gained by offering to the patient either real or fictitious blood-pressure figures. The level of the mercury seldom correlates with well-being. Hence the inconsequential fluctuations and the spontaneous variations of pressure so characteristic of essential hypertension are best recorded without comment. Neither doctor nor patient should be misled by blood-pressure readings. They are not an end in themselves.

In general, it may be said that therapy aims at preventing a further rise of pressure, and therefore at a reduction in the rate of wear and tear in the vascular system as a whole. By medical means it is seldom possible to lower blood pressure and even more impracticable to set it at an alleged ideal figure for the particular individual. In fact, the physician's endeavour in the great majority of his hypertensive patients past middle life is to help them to adapt their lives to the capabilities of their vascular systems. In older people it is futile to hope to modify the blood-pressure readings significantly. Longevity and comfort are promoted by adjustments in the way of living. In younger people at or under middle age more intensive measures are justifiable as the disease then is liable to run a severer and usually a shorter course.

#### TREATMENT OF THE INDIVIDUAL PAST MIDDLE LIFE

In the patient over fifty years of age or in those below this age in whom degenerative vascular changes are widespread, there is no doubt that symptoms are the best guide to successful treatment. In general, the quiet life recommended for the minor degrees of cardiac incapacity is applicable to the sufferer from this disorder. Long hours of work, domestic anxieties, emotional strain and the tension of competitive business, are aspects which may be considered with the patient, the doctor advising such restrictions as will allow of a definite routine without the production of further embarrassment. Should such measures in themselves prove insufficient to ease the patient, then it is wise that further limitations and restrictions be imposed. If economic circumstances allow, a prolonged rest or leave of absence from

work for three to six months is a desirable step. When this has been arranged, it is useful to recommend that from two to four weeks be spent in more or less complete confinement to bed, the sufferer having previously made such business arrangements as will free him from unnecessary anxieties of one kind or another. The success of this step depends not merely on physical rest but on the relief which comes from complete mental relaxation. The resolution of emotional conflicts, with the adoption of a calm and contented outlook on life and its problems, can do much to ease the burden on the circulatory system. A period of rest also gives an opportunity to make a full investigation of the general health and as accurate an assessment as possible of the state of the renal tract and the degree of vascular damage. After some weeks, outdoor exercise may be resumed gradually, but if symptoms continue, then it is probably wise that the man should be advised to retire from active participation in the rush and worry of a busy life. Too often retirement is postponed until it becomes synonymous with complete invalidism. On the other hand, there are those who only after many years of raised pressure begin to experience disagreeable symptoms. They are safeguarded by the provision of the restful life, the regular habit of long hours of sleep, the rest at midday, the quiet week-end and the protracted holiday. The lesson to be learned from this is that by adapting the daily routine to the blood pressure and the state of the vascular system as a whole, thus keeping symptoms in abeyance, much good can be accomplished over a period of time in middle-aged and elderly people, provided always that the emotional make-up of the patient is tempered by confidence.

**Diet.**—Dietetic measures have their ardent advocates, but there is no particular food the restriction of which will guarantee a fall in pressure. Many hypertensives tend to over-eat, and if this be associated with corpulence, then a clear indication for dietetic treatment does exist. One of the most successful measures in the care of the middle-aged patient is the correction of obesity by the continued use of a low calorie diet. Even 14 lb. in excess of the individual's standard weight for his age and height throws an unnecessary burden on the heart and circulation. The prescription of an exact diet of 1,500, 1,200 or 1,000 calories will do much to ease symptoms and increase the sense of well-being. Though the weight will fall, the blood-pressure levels are seldom significantly altered. Nevertheless, remarkable benefit may result. (See p. 383.) Dietetic treatment can only be successful in so far as the patient is prepared to co-operate. It should be explained that a loss of 1 to 2 lb. per week is sufficient. Consequently, according to his excess weight, many weeks of steady perseverance may be required. Weekly weighings are a good guide to progress and are worthy of more attention on the part of doctor and patient than the blood-pressure readings.

The benefits to be obtained by this method of treatment are so striking that even in those who are not grossly overweight, the cultivation of habits of restricted indulgence is well worth encouraging. There is nothing to be gained by a total restriction of red meat. Hypertensive people are usually blessed with good digestions and the colour of the meat is no bar to their enjoyment of it. The protein intake should be sufficient for bodily needs. Fresh fruits and abundant vegetables should form a large part of the diet, fluid should be taken in moderation and the minimum amount of salt taken which satisfies. The evening meal is better to be light and simple. Alcohol

need not be prohibited, but it is often wise to reduce or discontinue the habit of smoking.

**Drugs.**—In the absence of renal damage a small dose of calomel once a week followed by a saline purge has much to recommend it. When emotional tension runs high and there are obvious nervous influences at work, a small dose of bromide or phenobarbitone once or twice daily make useful remedies. Of the former, 7 to 15 gr. (0.42 to 0.9 gm.) in a mixture, and of the latter,  $\frac{1}{4}$  gr. (16 mg.) morning and midday, with  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) at night as a tablet, may be all that is required. Alternatively, the tablet phenobarbiton. et theobrom. (B.P.C.) may be ordered. This tablet contains phenobarbitone  $\frac{1}{2}$  gr. (0.03 gm.) and theobromine 5 gr. (0.3 gm.).

Vasodilator drugs have a very limited use in the treatment of hypertension. While nitrites have a reputation on experimental grounds, the reduction of blood pressure thus induced is only transitory and too short-lived to be of real benefit. No drug is known which has a permanent effect. Attempts to reduce the blood pressure by such means are usually ineffective, and when they do succeed, cause such disagreeable symptoms as flushing and throbbing in the temples that they must be abandoned. Amyl nitrite, nitroglycerin and sodium nitrite may be used during hypertensive paroxysms when energetic attempts to reduce the blood pressure from sudden dangerous levels are justifiable. Various vegetable substances such as extracts of mistletoe, either alone or in combination with insulin-free pancreatic and other organic extracts, are said to be the main ingredients of various expensive proprietary remedies. Critical studies have not substantiated the claims made for these preparations.

Potassium thiocyanate is capable of reducing blood pressure and has been used with success clinically, but the effective dose is usually so close to the toxic dose that there is only a narrow margin of safety. Toxic symptoms, which include weakness, lethargy, hallucinations, skin eruptions, with nausea and vomiting, hamper the use of this drug. The quantity appropriate for each patient must be carefully adjusted and determined with accuracy according to the level of the thiocyanate in the blood, which should not exceed 10 mg. per cent. In consequence the employment of thiocyanates in general practice can hardly be recommended at the present time.

Present-day conceptions of the pathogenesis of essential hypertension emphasize the importance of a humoral mechanism in the regulation of the arteriolar resistance. It is encouraging to know that recent work suggests that from normal kidney tissue a substance may be obtained which destroys or neutralizes the hypertensive effect of the pressor agent, angiotonin. The intensive investigations now in progress may yet supply the means of regulating blood pressure just as the judicious use of insulin can control the blood sugar level. Unfortunately, such renal hypotensive agents as have been prepared to date are not yet sufficiently dependable or reliable to warrant commercial distribution.

**Relief of Symptoms.**—*Headaches.*—Of distressing symptoms morning headache is often difficult to treat. In most patients admitted to hospital for this cause the headache clears up within a day or two by the provision of adequate rest and sleep. In more resistant cases relief can sometimes be obtained by correcting the patient's sleeping posture. By having the head of the bed elevated at night on 6-, 12- or 18-inch blocks, the headache



may gradually lessen and disappear after some days. The height of the bed should then be lowered to the optimum level. It is said that a reduced fluid intake in the later part of the day also helps to prevent morning headache. Occasionally a patient gets relief by sucking a tablet of glyceryl-trinitrate in a dose of  $\frac{1}{160}$  gr. (0.15 mg.) up to  $\frac{1}{100}$  gr. (0.6 mg.) or more on waking in the morning. If this is unsuccessful, as it often is, then recourse must be made to the more purely symptomatic analgesics, and for this purpose a full dose of phenacetin, 5 to 15 gr. (0.3 to 0.9 gm.) taken with a cup of hot tea on waking in the early morning, is generally very helpful. Tablets or powders containing aspirin, or calcium aspirin, with caffeine and phenacetin, are often useful. One man who had tried all the usual remedies without success assured the writer that he could prevent his morning headache by taking a tablet of ergotamine tartrate (Femergin) immediately before falling asleep the previous night. The wisdom of the continued use of such a remedy is certainly open to question in view of the dangers of ergotism. It is remarkable how on occasion a patient may remain free of headache for weeks on end after a profuse epistaxis or a generous venesection.

*Vertigo and Tinnitus* can cause much suffering. Sedatives are of most use. Bromides, chloral or barbiturates in small doses may be employed, but if ineffective after a short trial, a rest in bed for a few days may be suggested. The measures used in the treatment of headache may also be considered as worthy of trial, but it is disappointing to find how resistant this symptom may be in spite of all remedies.

*Hypertensive Encephalopathy* (cerebral crisis, acute cerebral oedema) is the term applied to the development of sudden severe but usually transient manifestations of cerebral vascular disease. Passing attacks of intense headache, convulsions, diplopia, monoplegia or hemiplegia, with rapid recovery, are symptoms and signs included under this term. Evidence for actual thrombosis or hæmorrhage is lacking. Simultaneously or preceding the attack the blood pressure is unusually high as a general rule. Local cerebral oedema due to increased capillary pressure is the mechanism usually held to be responsible for such seizures. Adherence to the principles of treatment already outlined is usually sufficient to prevent or at least reduce their frequency. The treatment of the actual attack aims at a lowering of intracranial tension and a prompt decrease of the local cerebral oedema. For this purpose lumbar puncture can only be undertaken with particular caution in view of the danger of a sudden decrease in pressure, permitting the medulla to be forced downwards into the foramen magnum, often with a fatal result. Hence not more than 20 c.c. of spinal fluid should be withdrawn, and this at a slow rate. The use of nitrites has already been mentioned. Amyl nitrite may be offered for inhalation to the unconscious patient, but as a rule the results obtained are disappointing. Epileptiform attacks should be treated with soluble phenobarbitone, 3 gr. (0.18 gm.) intramuscularly. McAlpine, having seen dramatic benefit result from the intravenous use of mersalyl (1 to 2 c.c.), recommends its use in the treatment of the acute manifestations of cerebral oedema. Similarly, the parenteral administration of hypertonic solutions of saline or sucrose described on p. 930 is of value in mobilizing tissue fluid and promoting diuresis. On occasions a prompt venesection may be life saving. This can be done by slitting open a vein at the bend of the elbow with a scalpel or a pair of scissors.



### SURGICAL MEASURES IN YOUNGER PATIENTS

In recent years increased attention has been devoted to the possibilities of relief of essential hypertension by surgical means. Such treatment is fully discussed on p. 672.

The present-day treatment of hypertension, whether it be medical or surgical, must remain symptomatic until such time as the energetic research now in progress in various parts of the world provides the physician with a more specific remedy and a rational plan of therapy. It ought then to be possible to prevent many of the serious complications of the hypertensive process. In the last stages of the disease, even before symptoms of cardiac embarrassment become pronounced and dyspnoea, fatigue and oedema complicate the situation, there should be no hesitation in employing digitalis, as this drug does not raise the blood pressure further and may do much to improve the circulation and ease the patient's distress. The treatment of the final stages when the heart fails and the systolic blood pressure begins to fall to a disproportionately low level, is to all intents and purposes that of congestive, dyspnoeic or anginal failure. Treatment of these forms of cardiac distress is fully discussed under the appropriate headings (p. 631 *et seq.*).

### CARDIOVASCULAR SYPHILIS

For the treatment of cardiovascular syphilis the reader is referred to the section on the treatment of syphilis and particularly to p. 225.

### THE SENILE HEART

Past middle life the individual is more than ever at the mercy of his arteries, and in elderly people, heart disease, the result of a slow and progressive narrowing of the coronaries, takes various forms. Hypertension is often present, and thereby increases the liability to angina or congestive failure. Treatment for these states will be found under the appropriate headings. In old age, with generalized arteriosclerosis, weakness of the skeletal muscles and diminution in the cardiac reserve advance step by step. The inability to take much in the way of physical exercise eases, to some extent, the cardiac burden. Congestive failure comes insidiously, often unexpectedly, and runs a short course.

The care of the heart and circulation in the elderly is based on the principles already described, particular attention being directed to physical activity. In such people the risks associated with a prolonged rest in bed are well known, basal congestion, infection and bouts of coughing being the main sources of danger to the heart. Exercise in the open air should be encouraged, sufficient to yield a natural fatigue as distinct from exhaustion and any undue degree of breathlessness. Irregular and spasmodic attempts should be avoided, and a definite amount of exercise in the form of short walks should be prescribed according to tolerance, a stated amount being accomplished day by day. In this way blood flow is improved, stagnation avoided and muscular tone enhanced. When circumstances permit, especially for those prone to bronchitis and respiratory catarrh, the winter months, being a source of danger, may be spent with profit on the South

Coast or abroad in milder climates favoured with more sunshine and warmth and a drier air than is to be found at home.

Diet in the aged presents problems peculiarly its own, but in general the secret of success is to be found in moderation. Balfour, acting on the principle that digestive processes are prolonged in the aged, used to insist on a minimum of five hours between meals, no solid food of any kind being taken in the interval. All invalids, and particularly elderly people, should have their principal meal in the middle of the day. It should be as dry as possible, thus diminishing the tendency to flatulence, and safeguarding the circulation from the absorption of bulky amounts of fluid. Salty articles and highly seasoned foods are for similar reasons best avoided. Alcohol has no value as a cardiac stimulant, but, as it increases a sense of well-being, and makes for bodily and mental comfort, there is no reason to countermand it in the elderly, who may be accustomed to its use in moderation. Diet will best be light, and adjusted so far as possible to personal idiosyncrasies.

A rest in the afternoon, a light meal in the evening and a long night's rest will often follow naturally. Sleep is to be encouraged. Hot milk or a whisky toddy taken some little time before retiring may be all that is required. Much insomnia and restlessness can be prevented by having the bed alongside a wide-open window. Fresh air as distinct from draughts should be made available in abundance. By such simple rules hypnotics are often unnecessary, but if adequate sleep is difficult to obtain the choice of a suitable drug demands consideration. Paraldehyde, were it not for its objectionable taste when taken by mouth, and its peculiar odour when exhaled, might more frequently be employed on account of its valuable properties. The taste can be disguised to some extent, particularly if dispensed in 20-minim (1.2 c.c.) capsules of which three or more make a suitable dose in the first instance, but its excretion is perhaps more embarrassing to the friends of the invalid than to the patient himself. Bromide, combined with a small dose of sodium phenobarbitone according to the prescription (p. 634), makes a gentle sedative remedy and often proves helpful to the elderly patient. Barbitone in 5-gr. (0.3 gm.) tablets or powders provides a stronger remedy, but in elderly people tends to be cumulative, and with constant repetition is occasionally responsible after a time for some minor degree of mental confusion. There is a form of sleeplessness not uncommon in the elderly which consists in a period of insomnia occurring for two or three hours in the middle of the night. These people have little difficulty in falling asleep when they first retire to bed, but in the morning are unrefreshed, as their sleep is broken. In the correction of this type of inter-nocturnal insomnia a rapidly acting barbiturate effective for an hour or two is a useful preparation to have available. Sodium amytal, in 3-gr. (0.18 gm.) capsules, is effective, as it comes into action in the course of fifteen to thirty minutes and the effect wears off in about six hours without any residual "hang-over." This drug can be taken through the night should the occasion demand its use.

Arsenic has some reputation in the treatment of the debility of old age, this being mostly based on the unconvincing evidence provided by the Styrian mountaineers who, having acquired a degree of tolerance to the drug, believe that it enables them to accomplish more work with less fatigue, less effort and less dyspnoea. In therapeutic doses arsenic has no direct effect on the heart or circulation, and any benefits which accrue from its

use in the elderly probably result from its "tonic" properties, in improving appetite and relieving weakness and apathy. It may be prescribed as liquor arsenicals (B.P.) in doses of 2 to 5 minims (0.12 to 0.29 c.c.) thrice daily after meals.

When bodily activity declines to such an extent that less and less can be accomplished, and when signs of basal congestion become evident, digitalis is indicated, and may be given in small doses of 15 minims (0.9 c.c.) of the tincture three times a day for a week or ten days at a time according to tolerance. If intermittent courses prove of value, then maintenance doses may be continued as necessary. Tablets of digoxin (0.25 mg.) are sometimes better tolerated by the elderly person whose digestion is impaired. When frank signs of congestive failure develop, special care must be taken in nursing with a view to the provision of the maximum amount of rest and comfort. The procedures outlined in the section dealing with the treatment of congestive heart failure are then applicable.

### HEART DISEASE IN RELATION TO PREGNANCY

Reference has already been made to the question of the selection of a suitable occupation for those afflicted by heart disease in early life. Of all careers maternity may be the most strenuous, particularly in a working-class household, and therefore advice may be sought regarding the suitability of the cardiac patient for the risks and responsibilities of marriage. Just as the contracting parties are unlikely to be dissuaded from their intentions, so it is as a rule unwise and unkind to forbid marriage, but the dangers must be explained to both parties. The probability is that the affected partner will die young. The man suffering from rheumatic heart disease will be debarred from life insurance, and in a short career is less likely to be able to provide adequate support for his dependants after his death. The woman faces peculiar dangers, for the available evidence suggests that even surviving the immediate burdens imposed on her heart by successive pregnancies her days are likewise shortened. It should be realized, however, that the great majority of young women suffering from rheumatic heart disease are able, in reasonably good surroundings and with skilled attention during the antenatal period, to bear one or at most two children without serious detriment, after which it may be considered justifiable to advise sterilization.

In no branch of cardiological practice is the ability to assess the degree of circulatory incapacity of greater consequence to the patient. Just as in the healthy woman minor degrees of cardiac embarrassment in the form of slight breathlessness and peripheral œdema often become apparent in the later months, so in the subject of definite cardiac disease a distinct aggravation of symptoms may be confidently anticipated as pregnancy advances. The outstanding danger is the development of congestive heart failure some time before term is reached. Labour under such circumstances is a burden which few will survive, and obstetrical interference undertaken in the presence of heart failure is the straw which breaks the camel's back. Pregnancy must be interrupted either in the earliest months in those likely to develop failure later, or, if it is allowed to proceed, adequate antenatal care and constant supervision must be made available throughout the pregnancy.

and labour conducted as expeditiously as possible. In determining appropriate treatment, the first duty of the physician is to correlate the degree of circulatory embarrassment in relation to the period of gestation. Atrial fibrillation adds to the gravity of the situation.

The degree of cardiac impairment is assessed on the ease with which symptoms of circulatory distress are induced. By this means the patient may be graded according to her functional capacity. Group I is composed of those women who have a structural cardiac defect, but who have no associated symptoms. In these women the cardiac lesion is commonly discovered in the course of a routine antenatal examination. Obviously the farther advanced they are in pregnancy with freedom from cardiac symptoms the better is the outlook. As a general rule these women will require no particular treatment, and will be able to accomplish a natural delivery, but they must be kept under observation at intervals of three or four weeks so that their cardiac state may be reassessed from time to time. As the burden of pregnancy increases they will tend naturally to develop symptoms as term approaches, and will thus tend to advance to the next group.

Group IIa is composed of those who have symptoms of a mild type—breathlessness and fatigue on heavier exertion. This degree of incapacity in the later months is not of serious significance, but up to the fourth or fifth month they likewise must be advised to report regularly for repeated observations. Treatment consists in the provision of adequate rest with longer hours of sleep. They should be advised to lie down for an hour or two each afternoon, have a long night's rest in bed and avoid fatigue. Such measures as these may be sufficient to check the natural tendency to further signs of distress, as exemplified by the next grade of failure.

Group IIb is composed of those who have very definite symptoms of breathlessness easily provoked. These women have been forced to decline their heavier household duties, and even with small amounts of exertion they exhibit breathlessness readily, and at night notice some swelling of the feet. This is an indication that particular care is required. Signs such as these occurring in the first three months warrant careful consideration, and usually the advice that the pregnancy be terminated, as by the time the sixth or seventh month is reached congestive heart failure of a more serious grade may be anticipated. Coming under observation about the middle of pregnancy a period of complete rest in bed for three or four weeks is desirable. It is often surprising to find how much good can be accomplished by this measure, particularly if every endeavour is made to ensure adequate sleep. There is probably no more important item in the care of these women than the correction of insomnia, and for this purpose the bromide and phenobarbitone mixture (p. 634) recommended in the treatment of heart failure is of the greatest value. At this stage sleep, sound and refreshing, can often accomplish as much or more than digitalis, and at the same time adequate doses of iron to correct the anæmia so common in pregnancy will often help considerably to restore circulatory function. The exhaustion of hyperemesis occasionally aggravates the cardiac state and interferes with drug treatment. Digitalis by the rectal route or digoxin intravenously (p. 641) may then be indicated. The symptoms of Group IIb in the later months are always a danger signal. These women require rest in view of the natural tendency of the symptoms, if unchecked, to advance

to congestive failure. Active measures in the form of enforced rest, sleep and digitalis are indicated.

Group III is composed of those who have signs of heart failure at rest. These women, even when confined to bed, are a little dyspnoëic, and have a degree of peripheral congestion more or less intense, ranging from a minor pitting œdema of the ankles to extensive anasarca and lumbar œdema. The essentials of treatment are absolute rest, careful nursing, a suitable diet and full doses of digitalis and mercurials. By this means an energetic attempt must be made to rid the patient of congestive heart failure before any obstetrical interference is attempted. With adequate supervision no pregnant woman should be allowed to advance to such a stage of heart failure, as it is of the most serious significance and is only aggravated by obstetrical interference. It is wiser to allow labour to proceed in the presence of congestive failure than to attempt the artificial evacuation of the uterus. In the latter instance she is almost certain to die, whereas with every attempt to support her heart and circulation by medical means she at least stands a chance of weathering the storm. Thorough treatment with a satisfactory response will then permit of Cæsarean section, at which time the opportunity may be taken, with the permission of the patient and her husband, to perform sterilization.

In these patients who have been suitably supervised throughout pregnancy, a successful delivery may be confidently anticipated. They should be admitted to hospital or nursing home a few days—perhaps a week—before term, provided with rest and sleep and, if necessary, digitalized by rapid dosage. During labour a sedative is usually indicated, such as  $\frac{1}{4}$  gr. (16 mg.) of morphia and  $\frac{1}{16}$  gr. (0.4 mg.) of hyoscine hypodermically. They should not be denied light anæsthesia. A protracted labour is to be avoided and the timely use of forceps frequently desirable. In the puerperium a longer time in bed will be compensated for by better health in the following months.

### CONGENITAL HEART DISEASE

Congenital defects in the architecture of the heart and great vessels vary enormously in the degree of incapacity which they induce. On the one hand there are those individuals advanced in years in whom during the course of a routine examination a hitherto unsuspected congenital abnormality of the heart or aorta is revealed. At the other extreme is the baby surviving perhaps only a few days, cyanosed even to a deep plum colour, dyspnoëic and distressed, for whom death is a merciful release. From a clinical point of view, more particularly with regard to prognosis, it is useful to classify congenital heart disease into three broad groups.

**Group 1.**—In the first group, the most severe, cyanosis is constantly present. Grave structural changes permit of mixing of venous and arterial blood within the heart. Pulmonary stenosis with a large septal defect is an example of such a condition. Here, as a general rule, the course is progressively downwards, and treatment, it must be confessed, can accomplish little. Such cases seldom pass much beyond the age of puberty, and as infants they demand special care in nursing. Nursing difficulties varying in severity are often present: the babies become dyspnoëic after feeding for only a short time. The usual arrangements have to be modified so that

they receive small amounts of a high caloric food at more frequent intervals, thus reducing the difficulties of the actual nursing. As age increases, despite every care regarding diet, nutrition in many cases fails, and these children are often under weight for their age. They are prone to infections, whooping-cough being a particular danger to the child with a congenital cardiac defect. Cold, fatigue and exposure should be avoided as predisposing factors, and every attempt should be made to increase resistance—ultra-violet light, cod-liver oil and malt and the avoidance of crowded places, particularly when infections are rife, help to decrease the liability to respiratory infections.

*Surgical Possibilities.*—An exact anatomical diagnosis in the presence of persisting cyanosis is often difficult, but this has not deterred the enterprising surgeon, who boldly offers a palliative procedure for such a formidable handicap. Blalock and Taussig, impressed by the importance of a diminution in pulmonary blood-flow as a cause of the continued cyanosis in this group of patients, recommend a reconstruction of the circulation so as to divert a greater volume of blood to the lungs. In Fallot's tetralogy, in which the cyanosis is partly attributable to the septal defect and partly to the stenosis of the pulmonary artery, the surgical anastomosis of a major artery—the subclavian or the innominate—with the pulmonary ensures a more adequate aeration of blood in the lungs and hence a reduction in the degree of cyanosis. Obviously, when cyanosis arises from causes other than diminished pulmonary flow, the construction of an artificial ductus of this type cannot be helpful. Such a procedure is certainly formidable and the results so far obtained, while impressive, are at the best palliative. It is questionable if an arterio-venous fistula of this type, resembling the naturally occurring patent ductus arteriosus, can increase life expectancy, though the immediate improvement in physical capacity is often remarkable. It is yet too early to form a considered judgment.

**Group 2.**—The second group is composed of those in whom cyanosis occurs only as a transient or terminal feature. In older children exercise only if taken to excess produces symptoms, or dyspnoea and cyanosis may be temporarily induced by bouts of crying in younger babies. This state of affairs is usually associated with an auricular or ventricular septal defect. In the absence of signs of cardiac distress on a reasonable amount of exertion no particular treatment or restriction of activities is desirable. It is a matter of adapting activities to the child's capabilities. Every attempt should be made to maintain a satisfactory state of general nutrition with freedom from intercurrent infection. It is probably true that in about half these cases a long life even of full activity may be enjoyed, but an equal number of patients often succumb before the age of twenty is reached, either as a result of congestive failure of the right-sided type or of subacute bacterial infection engrafted on the congenital anomaly. Adequate rest, the avoidance of a strenuous occupation and of unnecessary and unnatural fatigue all help to prolong life and make it more comfortable. Digitalis is indicated when congestive heart failure threatens, but so far as the septicæmic state is concerned little can be accomplished therapeutically. Bronchitis and pneumonia are a very real source of danger. The majority of these children have unfortunately to be regarded as invalids all their lives. Like the adult suffering from acquired heart disease they should have a long rest in the middle of the day, and slight ailments should receive every attention.

School is generally out of the question. A minority ultimately make better progress than might be anticipated, and after puberty can sometimes undertake light work.

**Group 3.**—The third or acyanotic group is the most important from the point of view of successful treatment. Symptoms are generally minimal or altogether absent and it is only by careful examination of the child, who has usually reached school age, that the defects amenable to surgical correction may be first revealed. Persisting patency of the ductus arteriosus, which unites the higher pressure system of the aorta to the pulmonary artery, is unaccompanied by cyanosis or finger clubbing but is productive of the characteristic continuous "humming-top" sound or Gibson murmur. Coarctation of the aorta, a curious obliterative stricture usually situated just distal to the left subclavian artery, can be recognized in the child by the absence of femoral pulsation in the groins. As children tolerate intrathoracic interference better than adults, the recognition and correction of these defects in early life is important. Surgery can successfully obliterate the patent ductus arteriosus and eradicate the stenosis of the distal aortic arch, both of which, while often virtually symptomless in early childhood, reduce life expectancy at least by half.

*Patent Ductus Arteriosus.*—The operation consists of ligation of the ductus as close to its aortic orifice as possible. In the hands of the experienced thoracic surgeon and with the co-operation of the highly skilled anæsthetist, the operative mortality should be 5 per cent. or less, despite the inaccessibility of the ductus, the transpleural approach and its close relation to vital structures.

Clinical experience indicates that this defect is seldom encountered after the age of 40, the commonest cause of death being a bacterial endarteritis in the pulmonary artery around the orifice of the ductus—until recently a uniformly fatal disease. Septicæmia, pulmonary infarcts, and a local Gibson murmur, are the main components in a diagnosis often missed. Surgical ligation in an exhausted and septic patient carries a mortality of 50 per cent.—a figure which the judicious use of penicillin combined with surgery at the earliest opportunity may yet reduce. Is it not better to forestall the killing complications of the patent ductus by ligating the channel in early life, preferably about ten years of age, when the child is relatively fit and capable of withstanding the procedure, than to postpone operation to a later age, when in the presence of a blood-stream infection and multiple lung infarcts, the operative risks are ten times as great? Early ligation of the non-infected ductus permits normal body growth, encourages adequate nutrition and prevents the development of a local infection without the risks of an uncertain invalidism which, extending over the years, becomes quite frequently the basis of a cardiac neurosis in addition to its physical handicap. With ligation successfully accomplished, the child can approach adult life with confidence and in full expectation of an unimpaired physical capacity. In older patients, on account of the operative hazards, surgery can only be justified when more severe symptoms warrant the risk.

*Coarctation of the Aorta.*—The operative procedure which has been practised in recent years consists in the excision of the constricted and obliterated segment of the aorta, and the reconstruction of the vessel by a continuous overting silk suture drawing intima to intima. In skilled hands

this type of end-to-end anastomosis has proved eminently satisfactory. When the arteries are young and resilient, and the proximal aorta unencumbered by degenerative changes, the operative risks are well worth taking.

## THE TREATMENT OF VARIOUS TYPES OF HEART FAILURE

For clinical and descriptive purposes it is useful to separate the end results of degenerative myocardial disease into three broad groups according to the predominant symptom. Thus it is that we recognize "Congestive Failure" in the presence of peripheral œdema, engorgement of the liver, and distension of the veins. Such a syndrome is frequently accompanied by breathlessness in some degree, but when the dyspnoea is predominant, acute and distressing and the peripheral congestion minimal, the failure is obviously rather different in type. For descriptive purposes it is justifiable to consider this latter form under the general heading of "Dyspnoic Failure." A further group is composed of those in whom pain of cardiac origin is the leading feature, either in the more protracted form associated with coronary thrombosis or in the recurrent paroxysmal type associated with effort. This distressing type of heart disease may be considered under the heading of "Anginal Failure." From a clinical point of view it is of interest to note that, while congestive and dyspnoic failure may be combined in the one individual, it is quite exceptional for congestion to consort with anginal failure, at least in the more acute forms. Dyspnoea, on the other hand, may be in evidence in anginal failure.

### CONGESTIVE HEART FAILURE

So far as the immediate treatment of this condition is concerned, it matters little whether the patient suffers from valvular or non-valvular disease of the heart. With few modifications the same measures are applicable to the young woman suffering from congestive heart failure secondary to old-standing rheumatic heart disease with valvular defects and aggravated by auricular fibrillation with a fast ventricular rate, as would be applied in the treatment of the same type of failure evident in the man past middle life with no valvular defect, but whose heart has laboured under the burden of a hypertension for many years, and whose peripheral congestion has been of more gradual onset. The fact that the treatment of the congestive failure is similar in each instance does not warrant the conclusion that the ætiological diagnosis for the cause of the condition can be neglected. When the functional capacity of the circulation has been restored and the congestion relieved, further treatment at the ambulant stage may very well depend on this very factor. While we cannot eradicate the cause of rheumatic heart disease, yet a subtotal thyroidectomy may well be indicated for the adequate treatment of congestive failure in the thyro-cardiac, and similarly a suitable course of antiluetic treatment when the ætiological agent is the *spirochæta pallida*.

There are grades of congestive failure, and it is not difficult to picture on the one hand the young rheumatic subject handicapped by extreme peripheral congestion, greatly swollen legs, ascites, hepatic engorgement and



perhaps some hydrothorax, exhausted, cyanosed and breathless on the least exertion. This is an extreme example. On the other hand, in the earliest stages, œdema will only be evident around the ankles towards evening. The first patient will require prolonged and thorough treatment at the earliest opportunity amounting to perhaps four to ten weeks in bed, whereas in the second instance a week's rest followed by advice regarding the restrictions of activity in the future may suffice.

#### GENERAL MEASURES

**Rest.**—Let us consider the more severe grade. At the outset it is wise to explain to the patient that absolute rest will be required, and that this implies confinement to bed for a number of weeks. Many a man will hesitate to submit to this advice on the grounds that he must put his affairs in order, and that he has certain business commitments which demand his personal attention. It is right to explain to him that half-hearted measures have no place in the treatment of cardiac disease, and that more will be accomplished in less time by a strict and complete régime than by temporizing with a serious situation. It can be explained to him that every phase of physical and mental activity increases the work of the heart, and that its burden can only be relieved by the provision of adequate rest. At the same time it must be realized that the full benefit of rest will be denied him if he is forced to retire to his bed with many business problems unsolved and surplus domestic or personal difficulties still preying on his mind. Depending on the circumstances, and guided by the severity of the symptoms, it is often justifiable to permit such a patient to do what he can in the course of a day or two to put his affairs in order, so that he may at once be rewarded by as complete a physical and mental rest as it is humanly possible to attain.

The patient should be put to bed—whether in his own house, a nursing home or hospital depends on many personal factors—and the practitioner familiarizing himself with the particular situation will judge whether adequate nursing care can be provided at home. The rest in bed must be absolute, and everything must be done to render the patient as comfortable as possible by the provision of a suitable number of pillows, support for the arms, a suitable amount of bedclothes and a warm but airy room. Many a patient will beg to be allowed to sit in an arm-chair, saying that his breathing is thereby rendered more free than when he is strictly confined to bed. As a general rule this reflects on the care which has been taken to give him the maximum amount of comfort when in bed. A support for the shoulders, a prop for the feet, a pillow under the knees are all devices which bring comfort, and when this is found the correct position should be maintained. The adjustable bedstead designed by Lewis for the nursing of cardiac patients has many advantages. By simple mechanical means the support for the back and shoulders is easily regulated to suit individual requirements. By a similar device the feet and legs can be lowered so that a semi-sitting posture can be maintained with freedom from strain and with the maximum amount of comfort.

For urination a bottle should be provided, and the only occasion on which the patient may be permitted to leave his bed is for bowel actions, and for this purpose a bedside commode should be provided. This concession cannot always be permitted, but it is useful to remember that many

patients, particularly heavily built and elderly men, expend much mental and physical energy in their unaided gymnastics to master the use of the bed-pan. The provision of a suitable commode at the bedside may result in less expenditure of energy. While there is much to be said for the disciplined routine of the hospital, yet in private practice the experienced nurse will so modify her methods as to avoid disturbing the patient as much as possible, particularly by wakening him in the early morning for washing and bathing. A meal can well be postponed should comfort be found in sleep.

**Sleep.**—A restful bed is therefore the first essential, but despite this, sleep is seldom as sound or as refreshing as in health unless active steps are taken to provide it. The correction of insomnia is of the utmost importance. Here again half-hearted measures are of little avail. Strangely enough there is often a peculiar reluctance to use opium or one of its derivatives in the presence of heart disease. As a hypnotic there is no drug to compare with it, and time and time again patients will say after an adequate dose that it has provided them with the first night's rest for weeks or even months. In the early evening the patient should be given hypodermically a dose of  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. (10 to 16 mg.) of morphine sulphate, and this repeated if necessary in four or six hours. An energetic attempt should be made to ensure a minimum of seven to nine hours' continuous sleep. This is so important that it cannot be overemphasized, for by this means alone it is often possible to restore in a remarkable way the efficiency of the heart and circulation. Every restless night prolongs the period of confinement to bed, and thus delays recovery. The cardiac patient as a rule tolerates morphia well, though vomiting occurring some hours after its administration is sometimes rightly attributed to the drug. If this be so, then some preparation containing the total alkaloids of opium may be substituted. The proprietary preparations of papaveretum (B.P.C.), containing 50 per cent. of morphine, have not the same tendency to induce nausea and vomiting as the single alkaloid—morphia. These drugs are useful and potent preparations. They may be taken in the form of tablets, each  $\frac{1}{8}$  gr. (10 mg.), by the mouth. When relief from insomnia in cardiac disease is urgently required, it is preferable that a dose of  $\frac{1}{3}$  gr. (0.02 gm.) be injected subcutaneously to ensure its rapid absorption. The comfort and peace of mind induced by these opium derivatives is usually profound, and after a few nights of refreshing sleep the dose may be reduced and some other reliable hypnotic gradually substituted. The combination of bromide with chloral is a time-honoured remedy, and is generally effective in heart cases. 20 gr. (1.2 gm.) of potassium bromide and 20 gr. (1.2 gm.) of chloral hydrate prescribed in a mixture may next be employed, the nurse having instructions to repeat the dose in three or four hours should the necessity arise. The potency of the bromide and chloral mixture can, if necessary, be enhanced by the addition of 10 to 20 minims (0.58 to 1.16 c.c.) of the tincture of opium or a similar quantity of nepenthe.

In recent years, on account of their reliability and ease of administration, the various barbiturate preparations have shown a tendency to replace the bromide and chloral mixtures of former days in the correction of cardiac insomnia. Phenobarbitone or its more soluble sodium salt may be given at night in doses of 2 gr. (0.12 gm.) in tablet form. Ampoules, each 1 c.c. of a 20 per cent. solution containing 3 gr. (0.18 gm.), are also available for *intramuscular* injection. This makes a convenient substitute for the sub-

cutaneous injection of morphia, which it may replace after the first few days. At a later stage either a mixture of bromide or one or more tablets of any reliable barbiturate (*e.g.*, butobarbital) may be taken by the mouth. Of these there are such a large number that the practitioner will be wise to familiarize himself with the effects of one or two well-selected remedies, or phenobarbitone can be combined with bromide as in the following prescription:—

R	Pot. Brom.	.	.	.	.	gr. xx (1.2 gm.)
	Phenobarb. Sod.	.	.	.	.	gr. $\frac{1}{2}$ (0.03 gm.)
	Liq. Arsen.	.	.	.	.	Mi (0.058 c.c.)
	Syr. Aurant.	.	.	.	.	Mxx (1.16 c.c.)
	Aq.	.	.	.	.	fl. dr. ii (7.2 c.c.)

Of this mixture 2 drachms (7.2 c.c.) in water taken in the evening is often sufficient to induce sleep, and, if necessary, one teaspoonful can be repeated as desired through the night should the occasion arise. In prescribing bromide for the insomnia of congestive heart failure, it is probably wise to avoid the use of the sodium salt, as the sodium ions favour the retention of water in the tissues. The inclusion of a small dose of arsenic is believed to reduce the liability to bromide skin eruptions.

During these first few days the doctor will visit his patient preferably twice in the twenty-four hours, and of these two visits the evening one is the more important, as at this time it is opportune to consider fully the provision of sleep. It is helpful to have the nurse keep a record from day to day of the hours spent asleep. It is worth aiming at a total of ten or twelve in the twenty-four as a minimum, but the drug selected and its dose will be largely determined by the patient's general condition, the amount of sleep obtained during the day and the degree of breathlessness, all of which are of greater importance than any physical sign revealed by examination of the heart.

**Diet.**—Having made provision for ample rest and for the correction of the insomnia, it is next advisable to draw up a definite dietetic scheme. Too often this is left to chance, and the experience or inexperience of the nurse who, in private practice, may know little of the culinary resources of the household. In hospital practice the routine diet of the ward must be frequently readjusted to suit the special needs of the cardiac patient.

In arranging a diet for his patient the doctor will bear in mind the desirability of restricting the total calories in order to reduce metabolism and decrease the work of the heart. On account of portal congestion large meals are badly tolerated; indeed, anorexia, nausea and vomiting often present special problems of their own. The restriction of protein to 50 or 60 gm. daily, an amount sufficient to compensate for nitrogen loss, reduces its specific dynamic stimulus to metabolism to negligible proportions. Fats as a rule are poorly tolerated, particularly so when jaundice—a fairly frequent accompaniment of the most advanced form of congestive failure—complicates the picture. Carbohydrate furnishes a ready supply of energy and is usually acceptable in an easily assimilable form. It can be given in sufficient quantity to make good the proposed calorie value of the diet. Patients suffering from congestive heart failure commonly complain of thirst. Fluid should be restricted to an amount sufficient to quench thirst. A strict fluid ration is unnecessary.

As a further principle the diet should be low in salt content, particularly salts of sodium, as clinical experience has taught that the sodium ion is of more importance than the chloride in the retention of tissue fluid. It is undesirable, even were it possible, to exclude entirely the consumption of sodium chloride, but a reduction to 2 or 3 gm. as compared with the usual intake of approximately 10 gm. per day in health is a useful step. Even with such a quantity the diet is apt after a time to become unpalatable, but the salt substitutes on the market are best avoided, as the majority contain sodium. It is as a rule sufficient to advise that salty and spicy articles of food be avoided, that as little salt as possible be used in cooking, and that salt be not served with meals. As a matter of experience, few patients begin to complain about lack of salt until the first week or ten days of treatment has been accomplished, by which time their thirst is usually relieved. Small quantities of salt may again be included in the diet for a few days, returning to the restricted sodium intake as necessary.

It is highly desirable that the food should be rich in vitamins, particularly vitamin B<sub>1</sub> and vitamin C, both of which, when administered in deficiency states, have a beneficial effect in the correction of cardiac œdema. Congestive heart failure occurring in the alcoholic, in whom the absorption of vitamins may be defective, often responds in a remarkable way to the parenteral administration of synthetic preparations of vitamins B and C.

For those adults who do not dislike milk, the Karell diet has much to recommend it, at least for the first few days of treatment. The procedure, which consists in its strictest form in the limitation of nourishment to no more than four glasses of milk, each approximately 7 oz., in the day, thus yielding a total of only 580 calories, is occasionally followed by brilliant results, the venous congestion subsiding, the œdema being relieved by a prompt diuresis, and a distinct amelioration of the patient's distress. There can be no doubt that were such a strict régime applied more often, greater progress might be observed in the first few days of rest in bed. This diet has the virtue that it restricts fluids, keeps the calories low, and reduces the intake of salt, but the frugality of these "meals" cannot be maintained for more than three or four days. In addition many patients dislike milk or find its monotony irksome. Any semi-solid food will therefore be appreciated, and this may take the form of soft-boiled eggs, crisp toast with unsalted butter, and fruit drinks flavoured with glucose. A diet of approximately 1,100 calories suitable for the average case and open to modification according to the tastes of the patient is composed as follows:—

#### DIET FOR CONGESTIVE FAILURE

Salt Poor. Restricted Fluid.

##### *Early Morning—*

Orange or other fruit juice with 1 teaspoonful glucose (total fluid, 3 oz.).

##### *Breakfast—*

- 1 egg—poached, boiled or scrambled.
- 1 slice crisp toast; butter; jelly marmalade.
- 1 cup milk.

11 a.m.—

Orange or other fruit juice with 1 teaspoonful glucose (total fluid, 3 oz.); *or*

Small glass of ovaltine or Horlick's (total fluid, 3 oz.).

Dinner—

Small helping pounded fish or sliced chicken or rabbit, or *tender* lean meat—may be served as soufflé or custard.

2 to 3 fingers fairy toast.

Stewed or baked apple or fruit whip, jelly or snow, with sugar.

Tea—

2 plain tea biscuits; *or*

Finger plain sponge—jelly if desired.

1 cup weak, freshly infused tea with milk and sugar.

Supper (not later than 7 P.M.)—

Stewed or baked apple or fruit whip or custard or curds or jelly with sugar.

2 tea biscuits or Dutch crispies.

9 p.m.—

Small glass of Horlick's or ovaltine or plain milk

Milk daily— $\frac{3}{4}$  pint.

All food should be cooked *without salt*, and no salt served with meals.

*Fluid*: Fluid content of this diet is approximately 800 c.c.

*Calorie Value*: Approximately 1,100 calories.

By adding a little cream (3 oz.) to serve with fruit, the calorie value would be increased to approximately 1,300.

The cream and butter of the diet ought to be adjusted according to the weight of the patient. As progress is made the quantities of food may be increased, but the total calories as a rule should not exceed 1,500 while the patient is confined to bed. When convalescence is reached, the diet should be so adjusted as to maintain weight at the correct standard for the patient's age and height. This is of particular importance, as even 1 stone in excess of the correct weight throws a considerable burden on the heart.

The diet outlined above being low in residue has little stimulant action on the bowel, though to some extent this is made good by the inclusion of quantities of fruit or fruit juice which may be increased or varied according to individual requirements. Nevertheless, purgatives will have to be prescribed by the doctor, and in their selection the previous habits of the patient have to be considered, recognizing that brisk purgation is exhausting and does little to relieve congestion. Diarrhoea should be avoided. A daily bowel movement is sufficient. A vegetable pill, perhaps one or more 3-gr. (0.18 gm.) doses of pill aloes (B.P.) at night followed by a saline purge in the morning, may be all that is required. A gentler stimulant which has much to recommend it in those not previously affected by a sluggish bowel is provided by the emulsion of paraffin and agar (B.P.C.) taken in a  $\frac{1}{2}$ -oz. dose in the evening. A glycerin suppository is in many ways preferable to the saline purge, which is necessarily associated with a large bulk of fluid. One glycerin

suppository may be inserted each morning, either a vegetable pill or the emulsion of agar having been taken the previous night. The stool which results is of almost normal consistency, and is unassociated with pain or colic. Many of the proprietary salines in common use contain sodium chloride or other salts of sodium, and though more agreeable to take than magnesium sulphate, are best avoided. For similar reasons, should an enema be required, 5 to 10 oz. of warm olive oil, to which one or two teaspoonfuls of turpentine may be added, slowly injected and retained for some hours is preferable to the discomfort associated with liberal quantities of soap and water. Taking into consideration the previous habits of the patient, the urgency of his present symptoms and the necessity for purgation, the doctor will then decide on the most suitable preparation for immediate use; further measures will be determined by the response obtained.

It is important to note that acting on the principles outlined above, remarkable improvement may become evident in the course of a few days. This is particularly true of patients admitted to hospital in varying degrees of congestive failure, who for one reason or another have been denied adequate supervision in their own homes. It is true that the nursing of the patient may make all the difference between success and failure, but it would appear that one factor determining progress which has been poorly assessed in the past is the provision of a better diet. The correction of under-nutrition and avitaminosis may well account for the prompt diuresis which often appears when the ill-balanced diet of the hospital clientele is corrected more or less automatically on their admission to the wards. Many patients thus treated will respond so satisfactorily that the administration of direct cardiac drugs is unnecessary, and indeed if the use of digitalis is postponed for a few days until progress has been observed, it helps considerably in assessing the prognosis. Even a partial diuresis induced by rest and diet without the use of digitalis betokens a favourable response to further treatment.

### THE THERAPEUTIC USE OF DIGITALIS

The proper use of digitalis may make all the difference in the treatment of heart disease. It is not a cardiac panacea, but no other cardiac drug is endowed with such propensities for good. A unique drug having peculiar properties of the utmost value in therapeutics, its use has to be mastered, and it can never be prescribed in a haphazard or aimless fashion. It is therefore essential to have a sound working knowledge of the mode of its action, the method of its administration and the results to be expected when it is given in adequate dosage for suitable periods at a time.

In the first instance it is useful to consider when digitalis therapy is indicated. The primary, and by far the most important, indication for the administration of this drug is congestive heart failure, however mild or however severe. It is of little or no consequence whether the blood pressure is high or low, whether aortic regurgitation is present or not or whether the heart-rate is fast or slow. If congestion is present, then digitalis is indicated beyond a doubt. It is true that when fibrillation is present, particularly if the ventricular rate is high—in the neighbourhood of 150 or thereabouts—a very satisfactory response to digitalis may be anticipated, but a slow,

regular pulse, even that of complete heart-block, is not a contraindication to its use when peripheral œdema and venous congestion are present. It is absolutely wrong to suppose that only those patients suffering from auricular fibrillation derive benefit from its use. On the other hand, a regular fast heart, such as occurs in the acute infections, notably pneumonia, or in thyrotoxic states, is not necessarily an indication for its use. Digitalis is also indicated in dyspnoic failure, being particularly useful in the prevention of attacks of "cardiac asthma," but yields little or no benefit in anginal failure, and is best avoided. Its administration in the paroxysmal arrhythmias is discussed under this heading. It is occasionally of advantage in the abolition of extrasystoles when these are troublesome to the patient, but they are not in themselves an indication for its use, nor when present do they necessarily contraindicate it.

From what has been said it will be obvious that the milder degrees of cardiac incapacity associated merely with breathlessness on exertion are not an essential indication for digitalis therapy, but it is sometimes difficult to determine the exact stage of cardiac insufficiency which warrants its use. The slightest forms indicated by some degree of breathlessness are usually amenable to restricted activities and longer hours of sleep and rest, and this is equally true of the mildest degrees of congestive failure, when œdema first makes its appearance towards evening. If such measures as rest and sleep in themselves are ineffective, then a certain indication for digitalis therapy may be said to exist. Smaller doses than in the more urgent cases are advisable, and as tolerance to this drug is never acquired its early use does not prejudice full doses should they become imperative at a later date.

It may therefore be said that the primary object in digitalis therapy is to relieve or prevent the characteristic symptoms associated with the two leading syndromes of myocardial insufficiency—congestive and dyspnoic failure. It is in these particular circumstances that real benefit may be anticipated from the use of the drug. If such symptoms of myocardial insufficiency as dyspnoea, œdema, increased venous pressure and congestion of the hepatic, pulmonary or peripheral circulation exist, then digitalis in adequate dosage is likely to be helpful. The use of the drug in the absence of such symptoms finds little or no support in clinical experience. Tachycardia in itself is no certain indication for digitalis. In brief, the object in using digitalis is not to slow the heart-rate, not to counter valvular defects, but to prevent and ease the symptoms of myocardial failure.

It is only natural that as a result of the known efficacy of digitalis a large number of preparations, official and proprietary, should be available for general use, but not all of these are of equal potency or proven efficacy. When digitalis is indicated, it is important to use a reliable preparation, and for this purpose there is none better than the tincture of digitalis or the powdered leaf which may be prescribed in the form of a freshly made pill or as a compressed tablet. It is a reassurance to know that in using the latter preparation all the valuable properties of the foxglove are offered to the patient at less expense than the single refined active and inactive bodies prepared by the manufacturing chemists and sold under various trade names. The pill or tablet containing  $1\frac{1}{2}$  gr. (0.09 gm.) of the powdered leaf has many advantages. The exact daily amount required is easily regulated, and for a maintenance dose the patient can carry it with him conveniently. The

tincture is equally effective, but it is said ultimately to deteriorate on keeping when dispensed in a watery solution. This is no real handicap to its use as relatively small amounts are dispensed at one time and deterioration only takes place in the course of years. *The dose should not be counted in drops from a bottle.* The size of a drop varies enormously, and it is an inaccurate way of administering the drug. When the pure tincture is in use it is preferable to have a single dose taken each day, say a measured drachm, rather than suffer the vagueness of twenty drops three times a day. Inexact digitalis dosage is fraught with danger to the patient, and confuses the doctor in his management of the case. For these reasons the powdered leaf, at least in private practice, is probably the best preparation to use. In comparing doses of these two preparations, the leaf and the tincture, it is useful to remember that  $1\frac{1}{2}$  gr. or 0.1 gm. of the leaf and 15 minims or 1 c.c. of the tincture are all equivalent quantities for clinical purposes.

It has been estimated that on the average the body destroys or excretes digitalis at a rate corresponding to  $1\frac{1}{2}$  to 2 gr. (0.09 to 0.12 gm.) of the powdered leaf or 15 to 20 minims (0.9 to 1.2 c.c.) of the tincture per day. When the daily dose exceeds this amount a proportion accumulates in the tissues, the concentration rising step by step until the excess overflows and the stomach rebels. To obtain maximum beneficial effects it is necessary to saturate the tissues with the drug, and in general the greater the body-weight the more digitalis is required for this purpose. Over-saturation is accompanied by symptoms of digitalis intoxication, but *the maximum therapeutic benefit is obtained by a concentration just short of the toxic amount.* From what has been said it must be obvious that if small doses are administered daily, say 10 or 15 minims (0.6 or 0.9 c.c.) of the tincture, an effective concentration of the drug in the tissues may never be attained, for just as much is eliminated or destroyed each day as is given to the patient. As a general rule seven to nine days will elapse before a daily dose of 60 to 90 minims (3.6 to 5.4 c.c.) of the tincture reaches a concentration sufficient to induce maximum benefit. By doubling this dose the time-lag is reduced to three or four days, as the drug accumulates more rapidly, and by trebling the dose the first symptoms of digitalis poisoning may be observed in twenty-four to forty-eight hours. Thus an effective concentration depends on the rate with which successive doses are administered.

For practical purposes it is useful to consider digitalis medication under two headings—the digitalizing dose, by which is meant the amount required to produce a full therapeutic response, and the maintenance dose, which is the quantity of the drug necessary to perpetuate and maintain the preceding digitalization with optimum benefit to the patient. The former dose is, in fact, an amount of the drug just short of that quantity which induces symptoms of intoxication. With few exceptions, the mildest symptoms of digitalis poisoning, such as headache and loss of appetite, are a better guide to adequate digitalization and the regulation of appropriate dosage than the rate of the pulse or the amount of cardiac slowing induced by the drug.

**The Digitalizing Dose.**—The patient is seriously ill and massive doses are to be employed. A patient who has not taken any of the digitalis group of drugs in the preceding fourteen days can safely tolerate an unusually large dose. Admittedly there are individual variations—some patients tolerating more, some less than the average quantity—but clinical experience teaches that advantage can be taken of the fact that full saturation or the digitalizing



dose depends chiefly on the weight of the patient and the potency of the preparation used. Tinctures of digitalis supplied by reliable firms in this country are now sufficiently standardized to correspond on the average with a strength of 1 c.c. to the "cat-unit." For example, a man of 140 lb. requires, on a theoretical basis, a total of 21 c.c. of the standard B.P. tincture in the course of twenty-four hours to produce a full saturation effect. It is not suggested that the digitalizing dose be calculated for each patient requiring the drug, or that it be administered in a single draught, but the calculation can be made quite simply according to the formula devised by Eggleston, who found that 0.15 c.c. of a standard tincture (1 "cat-unit" per cubic centimetre) per pound of body-weight, was the average dose required to produce full therapeutic effects. A patient of 140 lb. will therefore require  $140 \times 0.15 \times 1 = 21$  c.c. (315 minims) of a standard tincture or 2.10 gm. (32 gr.) of the powdered leaf. In using this method the total quantity thus determined is administered in suitable fractions over a period of twenty-four hours. For this purpose the tincture is particularly suitable, as the doses can be readily measured and administered at six-hour intervals, beginning with half the calculated total quantity (say, 10 c.c. or 150 minims) followed by one quarter, or a trifle more (say, 6 c.c. or 90 minims) followed by 3 c.c. (45 minims) and 2 c.c. (30 minims), each at intervals of at least six hours. The nurse who does not have a medicine glass graduated in the metric system or in minims can easily measure the dose of the tincture in a record syringe. If the principle be appreciated that a man of 10 stone requires as much as 21 c.c. or rather more than 300 minims of the tincture in twenty-four hours to produce a full effect, then the doctor may well make use of bolder doses than those commonly employed; in this way he will be able to secure rapidly the beneficial effect of full digitalization.

The method is safe and can be thoroughly recommended whenever digitalis is urgently required, *but it must not be employed if digitalis or an allied drug has been taken within the previous ten or fourteen days*, as serious toxic effects may then follow the first fraction of the massive doses if the tissues are already partially saturated with the drug.

The patient requires particular observation over the period of the drug's administration, and the attendant should be instructed to discontinue further doses on the first appearance of headache, anorexia or nausea. When a patient has not been treated recently with digitalis, half the total calculated quantity may be administered without the slightest misgiving. It is the later fractions in the series which require particular care in their use. Symptoms of intoxication are more likely to occur after the second, third or final dose, but on certain occasions, further doses in excess of the calculated theoretical requirements may be continued for several days before the first signs of over-saturation make their appearance. The nurse should be instructed to stop the administration of the drug on the first appearance of intolerance. Vomiting, usually preceded by the earlier and milder symptoms of intoxication, is a certain indication that too much of the drug has been administered. Vomiting should not be allowed to occur; it distresses the patient unnecessarily, and the retching induced, which may persist for twenty-four hours or more, imposes an unnecessary and undesirable burden on the circulatory system. Moreover, should maintenance doses prove to be desirable at a later date, the patient will naturally be prejudiced against the further use of the drug.

Various modifications of the original method of rapid digitalization have been applied in practice. A suitable plan is to administer a single large dose of the tincture, calculated on the basis of 1 minim (0.058 c.c.) to each pound of body-weight. In the first instance, a 10-stone (63.5 kg.) patient who had not previously been taking digitalis for at least a fortnight, would therefore receive 140 minims (8.4 c.c.). After a lapse of six hours, in the absence of the production of any toxic symptoms, 30-minim (1.8 c.c.) doses are commenced and continued at similar intervals until either toxic symptoms are induced or until a quantity equal to the original dose of 140 minims (8.4 c.c.) has been administered. Thus a man of 10 stone (63.5 kg.) would receive in succession at six-hour intervals 140 minims (8.4 c.c.), 30 minims (1.8 c.c.), 30 minims, 30 minims, 30 minims and, finally, 20 minims (1.2 c.c.) to complete the theoretical amount required for full digitalization. A simpler method which the practitioner may well employ and which has the virtue that it is devoid of all calculations, is to administer as a routine to those patients over 10 stone (63.5 kg.) in weight who are in need of digitalis, three successive doses, separated by six hours, of 90 minims (5.4 c.c.), 60 minims (3.6 c.c.) and 30 minims (1.8 c.c.) of the tincture of digitalis. If this is well borne, then 20 to 30 minims (1.2 to 1.8 c.c.) may be continued twice or thrice daily, as the occasion demands.

Of the pure refined preparations the crystallized glucoside, digoxin, isolated from the leaves of *digitalis lanata*, has a prompt effect, and is useful for rapid digitalization. In a patient of 140 lb. (63.5 kg.) or more, a single dose of  $1\frac{1}{2}$  mg. (six of the 0.25 mg. tablets in which it is conveniently dispensed), equivalent to 90 minims (5.4 c.c.) of digitalis tincture, may be taken by the mouth. In the presence of fibrillation it causes a rapid fall in ventricular rate, reaching a maximum in six to eight hours, at which time, in the absence of toxic effects, dosage may be resumed at a rate of one or two tablets six-hourly until maximum therapeutic benefit is attained. Digoxin has the advantage that it is probably absorbed more rapidly than a corresponding quantity of digitalis, and as its excretion rate is also more rapid there is less liability to sustained intoxication. On occasion, when symptoms are extremely urgent or when persistent vomiting precludes its oral use, it may be used intravenously (see p. 645).

When the patient's symptoms are less acute and circulatory incapacity more gradual in onset, rapid and intensive digitalization is less essential. Doses of 30 minims (1.8 c.c.) of the tincture thrice daily for two or three days, and subsequently 20 minims (1.2 c.c.) thrice daily for a similar or shorter period of time, may be all that is required. As a general rule the drug ought to be pushed until symptoms and signs of failure are relieved or until the mildest symptoms of digitalis intoxication supervene. With few exceptions, this is a better guide to adequate dosage than the heart-rate or the amount of cardiac slowing recorded. Whatever method of administration is selected, it is always wise to explain to the patient or his attendant that maximum benefit can only be obtained by an amount just short of that quantity which induces symptoms of intoxication. By explaining the procedure to the patient, his full co-operation is enlisted from the start of treatment. Too frequently the patient misinterprets the doctor's intentions and when maintenance dosage becomes necessary, unless he fully understands the situation, he is loath to resume the administration of a drug of which he may believe himself to be intolerant. Too often the doctor himself misinterprets the

situation, and when full digitalization has been induced by one preparation to the extent of inducing nausea or vomiting, he forms the erroneous opinion that the patient is intolerant to that particular variety of digitalis and substitutes a smaller dose of some less potent preparation.

Within twenty-four or forty-eight hours of complete digitalization, remarkable benefit may be observed. As a general rule comfort is found in longer and sounder hours of sleep, breathlessness lessens, diuresis begins and may continue quite profusely for several days, the body-weight falls—often surprisingly abruptly, and the venous pressure decreases. These are all obvious effects which can be readily observed and recorded from day to day. As a guide to the efficacy of digitalis therapy, records of body-weight and urine output are more helpful in assessing progress than the chart of the heart-rate. *It is insufficiently realized that the rate of the heart is not in itself a measure of the therapeutic response.* The importance of slowing of the heart-rate has been overemphasized, though in cases of auricular fibrillation, with a fast ventricular rate, this may be dramatic. When normal rhythm accompanies congestive heart failure, digitalis can act with full benefit without any appreciable alteration in the rate of the ventricles or with a decrease so slight—perhaps no more than 10 or 20 beats—as to have little or no influence on the therapeutic response, which actually may be just as brilliant and as satisfactory as in the patient with auricular fibrillation. While it is of advantage in congestive heart failure to have an excessively fast heart slowed and brought under control, the beneficial action of the drug on the muscle, whereby contractility is increased, far outweighs its other effects. The rate of the digitalized heart is at the best a poor assessment of the increased bodily comfort and restored sense of well-being, which are none the less real, though they defy accurate analysis and precise measurement. In other words, the dose of the drug should be regulated by the patient's sensations rather than by the rate of his heart.

**Maintenance Dosage.**—Having secured full digitalization and having noticed particularly the response of his patient to this procedure, the doctor will then decide on the necessity for a continuation of the full digitalis effect. The aim in maintenance dosage is to perpetuate a concentration of digitalis in the tissues just short of that amount which is capable of inducing intoxication. The secret of success is to be found in the use of the drug in short intermittent courses of a few days' duration. If the drug is prescribed in an adequate quantity the intelligent patient whose co-operation has been enlisted will soon learn to regulate his own dose much more effectively than his doctor is able to do. In the first instance the patient should be instructed to take the drug regularly day by day until the first appearance of headache or nausea is noted. The drug is then stopped for two or three days and a further course begun, when the same procedure is repeated. If the patient keeps a record of the number of consecutive days required to induce intoxication, he can soon learn to anticipate and avoid it by stopping the drug immediately before the first symptom is expected.

It is no solution of the problem to attempt to offer to the more fastidious patient some refined preparation of digitalis, or an allied body, in the hope that gastric disturbance may thereby be avoided. On the contrary, the patient is to be congratulated when he has determined for himself the exact quantity of the drug which he is capable of taking over a short period of time and which is associated with the first and slightest sign of digitalis

intoxication—namely, headache and a minor amount of dyspepsia. Intoxication of this nature is a certain indication that active digitalis principles are in use. By stopping the drug for two or three days, unpleasant symptoms rapidly subside, as the tissues become desaturated. A preparation said to be devoid of “irritant” properties is almost certainly inert so far as any desired action on the heart is concerned.

Pills or friable tablets of the powdered leaf, each  $1\frac{1}{2}$  gr. (0.09 gm.), provide a convenient method of regulating maintenance dosage, particularly in the ambulant patient, who can carry the drug with him, but in hospital practice the nurse usually measures the dose of the pure tincture in minims in a medicine glass at the bedside. A start may be made by ordering 15 minims (0.9 c.c.) of the tincture three times a day (or, for the ambulant patient, a  $1\frac{1}{2}$ -gr. (0.09 gm.) pill of the powdered leaf three times a day) to be taken regularly and discontinued on the first sign of intoxication. The first maintenance course of digitalis is begun as a rule on the third or fourth day after the digitalizing quantity has been determined—that is to say, on the fourth day after the first appearance of minor symptoms of intoxication, at which point the administration of the drug was originally discontinued. It cannot be too strongly emphasized that the exact quantity of digitalis required as a maintenance dose can only be determined by the method of trial and error. It varies considerably for different individuals, apparently being influenced to some extent by body-weight, just as is the original digitalizing dose.

The patient is instructed to note the number of days which elapse between the start of the maintenance dose of the medicine and its discontinuation. Whether the course of digitalis should be short or long depends largely on the quantity taken and on the interval between successive courses. Some people seem to do better on a short course of, say, five days than on a longer course of ten to fourteen days, before an intermission is necessitated by the first appearance of headache or nausea. In many ways a short course of five days with a pause of two days on which none of the medicine is taken has advantages as it lends itself readily to the patient's full co-operation. It becomes an easily remembered rule to omit all medication on two days, say, Saturday and Sunday, of each week. On the other hand, some patients prefer a longer course of ten or fourteen days, with an interval of three or four days. Each individual must learn to discover the method best suited to himself and from which he derives most benefit.

If the original course of digitalis amounts to more than a week, then the quantity of the drug taken daily may be increased by a dose of 10 or 15 minims (0.6 or 0.9 c.c.) in the second course, which will therefore tend to be shorter than the previous one. In this way it is usually possible so to adapt the doses that the drug is taken for five consecutive days, two days being omitted at the conclusion of each course. For similar reasons, should intoxication be induced in the first course after perhaps only three or four days' medication, then in a subsequent course a reduction of 10 or 15 minims (0.6 or 0.9 c.c.) in the daily dose will help to determine the quantity which the individual can tolerate for five days before the slightest signs of intoxication are experienced.

Too little attention is given to the regulation of maintenance dosage, and commonly the routine amount taken by the patient is too small rather than too large, with the result that he fails to get full benefit and becomes discouraged. By explaining the method to the patient, by arousing his

interest and by encouraging him to learn to regulate his own dosage according to his sensations, full digitalization can be maintained successfully for lengthy periods of time and the development of heart failure postponed or avoided.

With a clear understanding of the clinical use of the drug, difficulties in its administration are seldom encountered. It is quite exceptional in hospital practice to meet with a patient in need of digitalis in whom symptoms of general intoxication, nausea or vomiting, are induced by a quantity less than an adequate digitalizing dose, and yet in private practice there are occasionally patients who for one reason or another allege that they are intolerant of the drug. This may result from lack of supervision of the maintenance doses in a prejudiced and bewildered individual, or else it may be a peculiar personal idiosyncrasy. The latter must be rare and well worthy of accurate clinical study. Vomiting, which is the usual symptom of intolerance, may justify the substitution of the tincture for the powdered leaf, or vice versa, or 2 to 5 minims (0.12 to 0.3 c.c.) of the tincture of *strophanthus* or one of the more refined preparations such as tablets of digoxin (0.25 mg.), equivalent to 15 or 20 minims (0.9 or 1.2 c.c.) of the tincture, but it must be understood that digitalis or an allied preparation which fails to induce toxic symptoms in appropriate dosage is equally unlikely to be of benefit to the heart.

The nausea and vomiting of portal congestion, a common accompaniment of the advanced degrees of failure, is occasionally confusing in the regulation of digitalis dosage. Vomiting may thus be either a symptom of digitalis lack or of digitalis intoxication. Portal congestion sufficient in itself to induce gastric symptoms is almost invariably accompanied by a swelling of the liver and usually by ascites. Even if the drug is retained by the stomach its absorption is delayed and accumulation takes place more slowly. When congestive failure is present, the ventricular rate high and the auricles fibrillating, it may be taken that digitalis is indicated and that vomiting, if present, is not necessarily an expression of digitalis intoxication. From the point of view of digitalis therapy there are three alternatives. Full doses of digitalis may be continued by the mouth combined with 10 to 20 minims (0.6 to 1.2 c.c.) of tincture of opium to act as a gastric sedative, and thus promote retention of the drug, or digitalis may be given by the rectum, or finally an active preparation may be selected for intravenous use.

**Rectal Administration.**—When vomiting due to congestion of the gastric mucosa precludes the effective oral administration of digitalis, the tincture can be given in doses of 1 to 2 drachms (3.6 to 7.2 c.c.) daily by rectal injection. To reduce the tendency to local irritation and promote its absorption, the dose may be added to 2 or 3 oz. of 5 per cent. glucose saline warmed and injected slowly once each day. Rectal administration can be of the greatest value when the nausea and vomiting of a congested alimentary tract handicap the oral use of the drug. It is correct to say from personal experience of severe cases of hyperemesis gravidarum complicated by congestive heart failure, when little or no food could be retained by the stomach, that the rectal administration of digitalis by this method has yielded most gratifying results. The success of the rectal route usually becomes evident in a day or two, by which time the portal congestion subsides, and it is then possible to resume oral administration.

**Intravenous Administration.**—For intravenous use a choice may be made

between  $\frac{1}{40}$  to  $\frac{1}{30}$  gr. (0.25 to 1.0 mg.) of strophanthin or 0.5 to 1.0 mg. of digoxin suitably diluted. Intramuscular or subcutaneous injections of either of these preparations is to be avoided on account of intense local irritation and irregular absorption. The former is best given with the usual aseptic precautions diluted in 10 to 20 c.c. of sterile normal saline, and if attempts have been previously made to administer digitalis by the mouth the intravenous dose of strophanthin should not exceed  $\frac{1}{80}$  to  $\frac{1}{60}$  gr. (0.4 to 0.6 mg.). Thus used, a definite effect on the rate of the heart can usually be obtained within half an hour, and a full action in six hours. If gastric symptoms still persist, then a smaller dose than that formerly administered can be repeated in twelve hours, but great caution is required before a further dose is given, and in any case this should not exceed  $\frac{1}{80}$  gr. (0.4 mg.). For intravenous use digoxin is available in convenient ampoules, each containing 0.5 mg. in 1 c.c. of 70 per cent. alcohol. The effective intravenous dose is 0.5 to 1.0 mg. It must be diluted ten times with sterile saline immediately before use. This is most conveniently done by drawing up the contents of one or two ampoules into a 10 or 20 c.c. syringe, and completing the mixture by filling the syringe with saline to the correct amount. A full dose (1.0 mg.) will produce a decided effect on the heart-rate within ten minutes, and is maximal in two hours, but it must be borne in mind that a full intravenous dose can only be justified if it is certain that some other digitalis body has not been taken within the preceding ten days. When the patient is vomiting from time to time as a result of portal congestion, it is often difficult to know how much, if any, of the digitalis previously administered by the mouth has been retained. When intravenous therapy is used it is therefore wise to employ a small dose, say 0.5 mg. digoxin, and repeat this if necessary at intervals of six to eight hours, resuming oral administration at the earliest opportunity.

**Ineffective Preparations.**—There are other preparations of digitalis and digitalis bodies on the market, some of which are suitable for intravenous use, but it is true that not one of them is superior to a carefully standardized pharmacopœial preparation. Similarly, no benefit ensues from the hypodermic injection of  $\frac{1}{60}$  gr. (0.6 mg.) of amorphous digitalin, commonly used by the surgeons in states of circulatory collapse. Refined tinctures, said to be devoid of irritant properties and pure principles ardently advocated by the manufacturing chemists, are, with few exceptions, better avoided. The infusion of digitalis has so many disadvantages that its use has been practically abandoned. It deteriorates on keeping, and has to be given in a dose ten times that of the tincture to obtain the same result. While the whole of the active principles can be extracted in the infusion with special precautions, yet these are not often taken, and it therefore seems that the tincture or powdered leaf are definitely preferable. Tincture of strophanthus has little to commend it for routine use. In full doses its margin of safety is less than digitalis owing to its irregular and slow absorption. The writer has never seen conclusive proof that it was of benefit when digitalis had failed to give relief.

**Toxic Symptoms.**—Reference has already been made to the symptoms of digitalis intoxication, which may be grouped under two headings, general and local. It has been pointed out that the first to appear is almost invariably headache which is followed in definite sequence by anorexia, and some six or eight hours later nausea and vomiting if the usual doses are continued. Once induced, digitalis vomiting may persist for twenty-four or forty-eight

hours. It is peculiarly distressing to the patient on account of the associated retching, and it is harmful to him by the amount of exhaustion, fatigue and mental depression which accompanies it. Many patients are drowsy for the twenty-four hours or more following rapid digitalization, in spite of adequate sleep on previous nights. Diarrhœa, and in more pronounced cases of intoxication visual disturbances such as difficulty in focusing and the presence of yellow and green vision, may cause anxiety. In elderly men full digitalis dosage may be accompanied by mental confusion, a muttering delirium and hallucinations often taking the form of rectangular figures. The writer has seen these symptoms precede the more common digestive disturbances, and has found them all subside rapidly when the drug was discontinued for a day or two. The central nervous system is more susceptible to digitalis than the gastric mucosa. As regards local symptoms a close watch must be kept on the rhythm of the heart. A heart-rate below 50, the appearance of frequent extrasystoles, especially coupling of the beats, or the appearance of heart-block, either partial or complete, are all danger signals. The irregularity of partial heart-block is easily recognized by auscultation, and from the nature of things is only found when digitalis is administered in cases of normal rhythm. Complete heart-block, on the other hand, may occur either in patients with regular beating auricles or with auricular fibrillation: in the latter instance the heart becomes regular, and when due to digitalis the dissociation usually leads to a ventricular rate higher than that found in complete heart-block of arteriosclerotic origin. The complete heart-block of digitalis is less frequent than commonly supposed, and when first recognized the ventricular rate is usually about 50 per minute, though higher rates are occasionally observed, particularly if the administration of digitalis is continued, whereas a rate in the neighbourhood of 30 is usual in the arteriosclerotic variety. A more serious and more common indication of digitalis intoxication is the development of a ventricular tachycardia. This occurs as a rule in arteriosclerotic patients, the subjects of advanced myocardial degeneration in whom the response to digitalis has been unsatisfactory with the result that its administration has been pushed to excess in the hope of relieving the congestive failure. It is recognized by the sudden development of an excessively fast ventricular rate usually in excess of 180 per minute. It is accompanied by a marked pulse deficit, so that it may pass undetected unless attention is paid to the rate of the heart. Its persistence for more than a few hours generally leads to an advance in the degree of congestive failure, and the fall in blood pressure which usually accompanies it may be partly responsible for cerebral symptoms ranging from mental confusion to epileptic convulsions. Ventricular tachycardia is a serious sign which usually betokens a fatal issue. The abnormalities of rhythm are more likely to occur before the general manifestations of intoxication in advanced degrees of congestive failure.

There is no specific treatment for digitalis intoxication beyond the obvious necessity of omitting its further administration. The prescription of a dose of castor oil, with the intention of emptying the alimentary tract and thus avoiding further digitalis absorption, often helps to relieve the patient when the drug has been given by mouth. For excessive intravenous therapy there is no remedy. The intravenous route is, therefore, not without danger, particularly if the patient be already even partially digitalized.



**Summary.**—To summarize the principles outlined in preceding paragraphs, it will be appreciated that having a clear indication for the use of digitalis it is the duty of the doctor to ensure that the patient receives an adequate amount in as short a time as the urgency of the symptoms demands. Its successful use involves accurate and repeated clinical observation with a close and careful study of the patient, both in regard to the drug's beneficial effects and its peculiar toxic symptoms. Its mastery ripens clinical experience and yields a satisfaction to doctor and patient with which few other drugs can compete. To perpetuate the beneficial effects thus induced, maintenance doses are usually necessary. Taken in short courses of a week or less with an intermission of two or three days, the drug can be regulated so as to yield maximum benefit over long periods of time without the production of toxic symptoms. Maintenance dosage cannot be controlled effectively merely by the consideration of the pulse-rate.

### THE USE OF DIURETICS

**Organic Mercurials.**—Drugs which produce a profuse flow of urine are indicated in the treatment of congestive heart failure when, after a fair trial, the response to digitalis is incomplete or unsatisfactory. From what has been said previously it can be judged that they are only required in a proportion of cases, and that this proportion decreases with the thoroughness with which digitalis is used. If after full digitalization and adequate maintenance dosage for a week or ten days œdema and venous congestion persist, or, as sometimes happens, increase despite the slowing of pulse-rate induced by the drug, then diuretics are to be considered. A large number are available, from which it is not difficult to make the appropriate selection. Clinical experience indicates that of all the diuretics available for use in the treatment of congestive heart failure, there is none to compare with the organic mercurials. In cases of advanced congestive failure it is a waste of time to temporize with the saline diuretics such as potassium citrate and acetate in doses of gr. xv to xx (0.9 to 1.2 gm.) by mouth, though highly thought of by the clinicians of fifty years ago when little else was available to them. If diuretics are really required, then it is right and proper to use potent and reliable remedies of known efficacy. For this purpose the injection of mersalyl (B.P.) cannot be bettered. This preparation, which is dispensed in a 10 per cent. solution in 1 or 2 c.c. ampoules containing a 5 per cent. solution of theophylline, is administered intramuscularly or intravenously on alternate days. It is usual to commence with a small dose, perhaps 0.5 c.c. by the intramuscular route. In giving the drug, a better effect is obtained when the injection is made into an œdema-free area, and it is important that the solution be deposited as deeply as possible, and that none escape under the skin, for in the latter situation it may give rise to intense local irritation which may pass on to the formation of a sterile abscess, sloughing of the superficial tissues and local ulceration. A useful site for the injection is the gluteal region, or if this is œdematous then the drug may be deposited in the scapular muscles. Injections in the region of the deltoid muscle or upper arm are usually very painful, and this site should never be selected when mercurial salts are in use. After the injection is completed the site ought to be vigorously massaged with a ball of cotton-wool, as this diminishes the local irritation which commonly persists for half an hour or more after the drug's



administration. Despite the selection of the gluteal region some patients complain of great pain around the site of the drug's injection. If local massage is insufficient to prevent discomfort, it is permissible to add 2 or 3 minims (0.12 or 0.18 c.c.) of 2 per cent. sterile procaine solution to the syringe already loaded with the mercurial preparation. The efficacy of the mercurial diuretic is not impaired by the addition of the local anæsthetic, which even in a dilute form is very effective in preventing all discomfort. Thin and elderly people appreciate this combination.

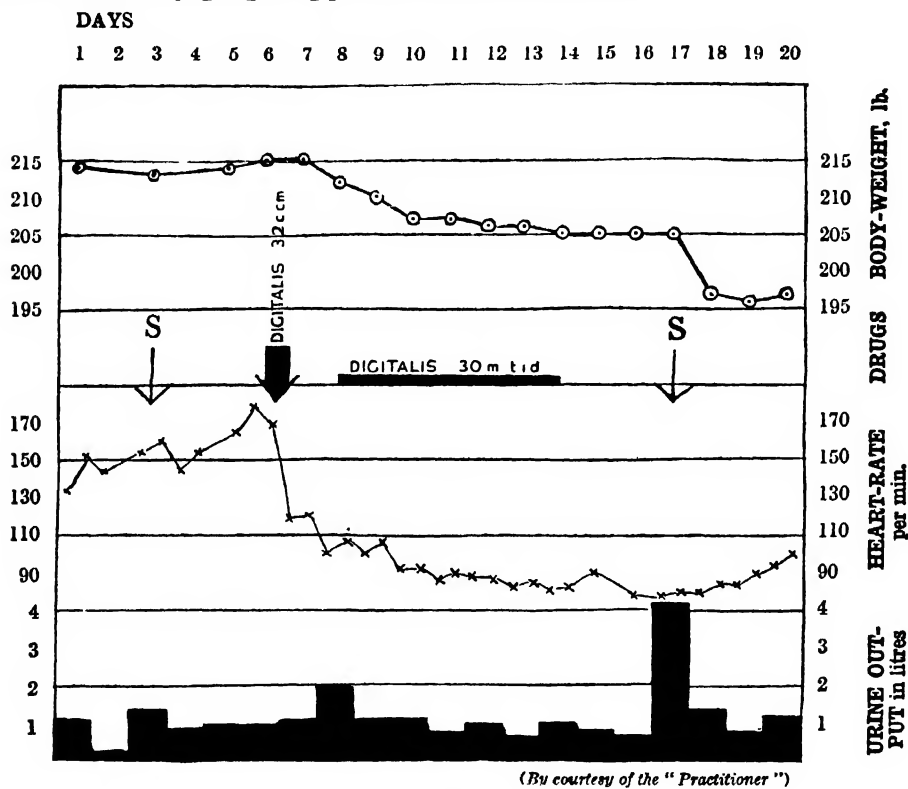


FIG. 5

Graph showing the effect of massive doses of digitalis tincture in a man, aged forty-six, 215 lb. in weight, suffering from congestive heart failure with auricular fibrillation. He received successively 15, 8, 5 and 4 c.c. at intervals of six hours on the sixth day of observation without the production of intoxication. He had a remarkable tolerance for the drug, as two days later 30 minims (1.8 c.c.) was begun thrice daily and continued for six days, when nausea was first induced. The fall in body-weight amounted to 10 lb. It is noteworthy that digitalis potentiates the effect of salyrgan or mersalyl (S). Compare the effect on body-weight and urine output of the dose of 2 c.c. on the third day with that on the seventeenth, when the man had been digitalized.

Successive doses on alternate days may be gradually increased up to a maximum of 2 c.c., and may be continued at weekly or bi-weekly intervals, if the occasion demands it, for many months at a time. On the other hand, if the response to intramuscular injection is judged unsatisfactory, then recourse is made to the intravenous route. For this purpose a vein at the bend of the elbow is usually selected, and with the customary aseptic precautions the drug is slowly injected diluted in 10 or 20 c.c. of normal saline. Novurit is a mercurial compound dispensed in suppositories containing 0.5 gm., and in 1-c.c. ampoules (0.1 gm.) with 0.05 gm. theophylline for

intramuscular or intravenous use. The suppository is generally an effective, easy and painless method of administering the diuretic, but it may give rise to intense irritation in the presence of local rectal disease. Internal hæmorrhoids or fissures may preclude this route of administration on account of acute discomfort usually experienced an hour or two after the suppository has been inserted.

The response to these drugs is often so dramatic that there is much justification for the claim that the modern use of mercury in the treatment of congestive heart failure represents the greatest advance since Withering's account of the use of digitalis in 1785. The diuresis induced by any of these preparations commences within two hours, reaches a height in eight or twelve hours and is usually completed in the course of twenty-four to thirty-six hours. The actual response depends on a number of factors. It is greater when full digitalization is maintained, and is more abrupt and complete when the intravenous route is used in preference to the delayed absorption which must result when the drug is deposited into an œdematous area. The volume of urine excreted must also depend on the dose employed and the degree of congestion and œdema existing at the time of its administration. In a digitalized patient in whom an advanced degree of œdema persists, a full dose of mersalyl intramuscularly may induce an enormous diuresis amounting to 3 to 5 litres in the twenty-four hours following its administration, and the fact that similar doses may be repeated at intervals of two or three days with safety indicates the potency and suitability of these mercurial drugs in the treatment of the more severe grades of congestive failure. They are therefore a useful adjunct to digitalis therapy, not merely in resistant cases but also in those patients who may still have a degree of occult œdema after adequate digitalis therapy. It is not uncommon to find that after all clinical evidence of pitting œdema in the subcutaneous tissues over the sacrum or thigh has disappeared, a single dose of mersalyl may still induce a minor diuresis and corresponding fall in body-weight. The drug may therefore be given to supplement digitalis therapy in any case of congestive heart failure. In the more severe grades it will rid the tissues of excess fluid when repeated at intervals of a week or two during the ambulant stages of treatment. The oral administration of mersalyl in pellets, each containing 0.08 gm., is a procedure at present under trial. Further experience may establish the usefulness of this method as a means of supplementing and maintaining the beneficial effects of intramuscular or intravenous injection.

By its action on the renal cells mersalyl is contraindicated in the presence of parenchymatous nephritis. Serious and even fatal reactions are occasionally noted when it is used in this condition, especially when it is given by the intravenous route. Mersalyl should also be used with caution when renal function is greatly impaired in the chronic interstitial form of renal disease. The assessment of renal damage in the presence of congestive heart failure is always a difficult problem, as albumen and casts in the urine may equally well result from passive congestion of the kidneys as from a true nephritis, but the clinical history, the blood chemistry and particularly in practice the specific gravity of the urine usually help considerably in determining the presence or absence of actual renal disease, a high specific gravity indicating satisfactory renal function.

**Ammonium Salts.**—In virtue of their powers of inducing acidosis, ammonium nitrate or ammonium chloride are both mild diuretics which

may be used to augment the effect of the mercurial compound when the response to the latter is judged incomplete or unsatisfactory. They are usually unnecessary, but can be prescribed for a week or ten days at a time in doses of 15 to 20 gr. (0.9 to 1.2 gm.) four times a day. Owing to their objectionable flavour these drugs are best prescribed in cachets or enteric-coated tablets, each  $7\frac{1}{2}$  gr. (0.45 gm.), but an attempt may be made to disguise their taste in a mixture by including liquid extract of liquorice or syrup of orange, as in the following prescription:—

R	Ammon. Chlorid.	.	.	.	gr. xv (0.9 gm.)
	Ext. Glycyrrh. Liq.	.	.	.	℥xxx (1.8 c.c.)
	Sp. Chlorof.	.	.	.	℥x (0.6 c.c.)
	Aq.	.	.	.	fl. oz. $\frac{1}{2}$ (14.2 c.c.)

Sig.—t.i.d.  $\frac{1}{2}$  fl. oz. (14.2 c.c.)

An effective method is to use these salts of ammonium on the day preceding the dose of the mercurial. They can then be stopped for two days and repeated as necessary. Alternatively, another method is to prescribe a single 30 gr. (1.8 gm.) dose two or three hours before the mercurial injection. Out of consideration for the patient it is always preferable to administer mercurial diuretics in the morning, as if given later in the day the massive diuresis is liable to interfere with sleep.

**Xanthine Diuretics.**—It is unnecessary to say much regarding the use of the xanthine diuretics, caffeine, theobromine and theophylline (theocine), as these have largely been displaced by the more powerful and efficacious mercurials. Theocine is the most powerful diuretic of the group, and owing to its insolubility is best prescribed in doses of  $2\frac{1}{2}$  to 5 gr. (0.15 to 0.3 gm.) in tablets or powders. Theophylline sodium acetate, a more soluble salt, may be prescribed in mixtures, but is liable to induce nausea and vomiting. Theobromine sodium salicylate has also a certain reputation in the treatment of cardiac dropsy, and as it is freely soluble in water it may be prescribed in doses of 10 to 20 gr. (0.6 to 1.2 gm.) in a mixture three or four times in the day. If after a trial of five to seven days these diuretics produce no appreciable benefit, they are best discontinued, but may be resumed again after an interval of a week or thereabouts. Theophylline has been combined with ethylenediamine (as in the proprietary preparation aminophylline), and when given orally in doses of 0.1 to 0.2 gm. thrice daily in tablet form it is occasionally useful on account of its diuretic properties. The natural diuretic urea, in doses of 15 to 30 gm. by the mouth, has also been advocated, but is less efficacious in cardiac dropsy than the mercurials or the xanthine compounds.

**Vitamins.**—Recent clinical work has conclusively demonstrated that cardiovascular disturbances are of frequent occurrence in vitamin-deficiency states. These occur commonly in alcoholic subjects, due to defective absorption, and in non-alcoholics as a result of an unbalanced diet or after acute infections when the vitamin requirements are increased by a high metabolic rate. Beriberi in the wet form is the classical example, but it must be understood that minor degrees associated with multiple deficiencies are of common enough occurrence throughout the general population of non-tropical countries. It is for this reason that vitamin concentrates, particularly vitamin B<sub>1</sub> and vitamin C, may be of striking value in the treatment of congestive failure with or without valvular disease. As vitamin B<sub>1</sub> deficiencies are frequently associated with gastro-intestinal and hepatic

disorders, it is advisable to administer the synthetic substance parenterally in doses of from 5 to 20 mg. twice or thrice daily. This dose is open to modification, because as yet there is insufficient information on the daily requirement of this vitamin, its storage and its utilization. Its administration is usually associated with diuresis, slowing of the pulse and elevation in the arterial pressure. Vitamin C has diuretic properties even in health, and, administered to patients with congestive failure in tablet form as ascorbic acid (B.P.), each 50 mg., three or four times a day, is capable of inducing and maintaining a profuse diuresis even when other therapeutic measures have failed. Vitamin C deficiencies are more common than formerly supposed, and when present usually respond promptly to full doses by the mouth, or the synthetic preparation may be given parenterally in doses of 100 to 500 mg. It may actually induce a diuresis in excess of that produced by digitalis, though not with the same degree of clinical improvement nor with reduction in the ventricular rate. When the response to digitalis is incomplete the probability of the presence of a vitamin deficiency should be borne in mind, as it may be readily corrected by full doses of ascorbic acid or vitamin B<sub>1</sub>, and the patient can be maintained in good health by adequate vitamin intake readily provided by the consumption daily of fresh food rich in vitamins.

### MECHANICAL PROCEDURES

**Venesection.**—Of mechanical methods of treatment one of the most important is the old remedy of venesection, which so often produces even within a few minutes striking benefit to the cardiac patient. Its use has tended to be neglected in recent years, with the result that the precise indications for its employment are difficult to determine. It is certainly true that most benefit is likely to accrue from this method when both the arterial and venous blood pressures are raised, though there are exceptions even to this rule, as striking benefit may result in the acute forms of left-sided failure with pulmonary oedema when there is little or no engorgement of the neck veins. It is contraindicated in the presence of anæmia or a low arterial blood pressure. When the liver is acutely engorged painful or pulsating, and there is much cyanosis and pulmonary oedema, the procedure may generally be used with considerable benefit, and this increases the more rapidly the blood is withdrawn. In urgent cases it is only necessary to incise an engorged vein at the region of the elbow and allow the blood to spurt. A needle of as large a bore as can be inserted into a vein may be used as an alternative, a tourniquet being lightly applied round the upper arm. By this means 300 to 600 c.c. of blood may be rapidly withdrawn. It is a method of treatment which opens a wide field for further investigation as regards its beneficial effects, the indications for its use and the development of an improved technique such as might be accomplished by the adaptation of suction methods to increase the rate of blood loss, either by a modification of the Potain aspirator or by a foot pump. The sudden withdrawal of blood eases the burden on the right side of the heart, diminishes pulmonary and hepatic congestion and often appears to permit an improved response to digitalis therapy. The method is certainly less efficacious in long-standing cases of heart failure when, after months or years, cirrhotic changes have occurred in the liver and other organs.

**Paracentesis.**—Hydrothorax or ascites seldom warrant mechanical interference until a fair trial has been made with other methods of treatment. Fluid at the base of either lung is a common occurrence in congestive failure, and may on occasions be bilateral. If it is resistant to treatment and the chest more than half full, then a two-way syringe is a convenient method of withdrawing it. At the conclusion of the paracentesis the injection into the peritoneal or pleural cavity of 1 to 2 c.c. mersalyl suitably diluted is a procedure which has been practised, but has little to recommend it, as the mercurial is probably not absorbed any more freely from either cavity than after its intramuscular injection. The mechanical removal of large quantities of fluid from either the thorax or peritoneum often appears to expedite recovery.

As a last resort it is sometimes justifiable to insert three or four Southey's tubes subcutaneously into the swollen legs, usually in the neighbourhood of the ankle. If this procedure is adopted a more satisfactory drainage results if the legs are kept pendent, the excess tissue fluid being thus displaced to the periphery by the force of gravity. Large quantities of oedema fluid can be removed by this method, or through multiple incisions made in the skin, due precautions against sepsis being taken. Copious absorbent dressings are necessary. The danger of sepsis has probably been over-emphasized, but the method is one more adapted to hospital than private practice. As a general rule only temporary benefit results.

#### SYMPTOMATIC TREATMENT

**Cough and Pain.**—The measures already described are in themselves usually sufficient to ease the patient's discomfort, but from time to time other symptoms arise for which relief is sought. Amongst these, cough, attributable to the pulmonary congestion, is often trying to the patient, particularly when it occurs in repeated paroxysms, and tends to interfere with sleep. As congestion subsides under the influence of digitalis and diuretics, bouts of coughing as a rule become less frequent, but should they in themselves place a burden on the heart and fatigue the patient a gentle sedative cough mixture may be prescribed. For this purpose 2 to 4 drachms (7.2 to 14.4 c.c.) of the Brompton mixture,<sup>1</sup> repeated if necessary, is a suitable remedy. On the other hand, chronic bronchitis with an asthmatic element occasionally complicates congestive heart failure, and in these circumstances a cough mixture of a more stimulating type incorporating a small dose of ephedrine hydrochloride is often helpful. On account of its stimulating properties to the sympathetic system ephedrine, however, is best avoided until a satisfactory response has been recorded, and even then is only to be used with caution. Pulmonary embolism or thrombosis may give rise to considerable pain if there be an associated pleurisy, and the hæmoptysis which commonly accompanies the infarct may cause a good deal of mental anxiety. From both points of view, morphia is the best drug to employ in the first instance: later the pain may be soothed by hot applications in the form of fomentations or antiphlogistine poultices.

**Oxygen therapy** has as a rule only a limited application in the treatment of circulatory disease. It will do nothing to correct cyanosis which results

<sup>1</sup> Brompton mixture :—

R	Liq. Morph. Hydrochlor.	.	.	.	fl. dr. 1½ (5.4 c.c.)
	Acid Hydrocyan Dil.	.	.	.	fl. dr. ½ (1.8 c.c.)
	Syr. Tolu.	.	.	.	fl. oz. 1 (28.4 c.c.)
	Inf. Ros. Acid. Rec.	.	.	.	fl. oz. 6 (170 c.c.)

from circulatory stasis in the periphery. On the other hand, pulmonary congestion and œdema of the alveolar walls may interfere with the normal oxygenation of hæmoglobin in the lung capillaries. This lends itself to treatment if it is possible to increase the partial pressure of oxygen in the lung alveoli. It can be realized that both factors, pulmonary congestion and peripheral stasis, frequently coexist. The final test of the value of oxygen is the effect of its administration to the patient. If the cyanosis promptly disappears when oxygen is inhaled in sufficient quantity, then its use should be continued, usually with benefit. It is only worth while persevering with oxygen therapy if the patient derives real benefit and can comfortably tolerate the method of administration. Dyspnœa is often apparently lessened by its use. The technical details of oxygen administration are described on p. 954.

### CONVALESCENT CARE

When peripheral œdema has subsided, and it is obvious that the patient has regained strength and is sleeping comfortably at night, he may be allowed to leave his bed and sit in a chair for gradually lengthening periods. Twenty minutes or half an hour is usually sufficient in the first instance. This period may be increased by fifteen minutes daily, provided it is unaccompanied by any undue fatigue or a return of peripheral congestion. After ten days or a fortnight he may be permitted to walk short distances in his room, and later, depending on economic circumstances, a resumption of duty may be considered. It is almost invariably necessary that a patient who has suffered from congestive heart failure should have his activities greatly curtailed. For many months it is a wise rule to insist that the week-end should be spent resting, if not entirely in bed, and that at the most only half a day's work should be attempted. Those in a more secure financial position should be advised to retire from active business. The details of drug treatment depend on circumstances, and these are discussed under the heading of *The Management of the Ambulant Cardiac Patient* (p. 615).

### PULMONARY DISEASE IN RELATION TO HEART FAILURE

Acute right ventricular failure is the term employed to describe the group of symptoms—urgent dyspnœa, chest pain and retrosternal oppression—associated with the impaction of a major pulmonary embolus. An enormous burden is thus abruptly thrown on the right side of the heart. Local thoracic distress is associated with considerable collapse and shock. Morphine should be administered generously at once, and the peripheral vascular disturbance countered by reassurance, warmth, elevation of the foot of the bed, and the free administration of oxygen. The use of peripheral vascular stimulants such as nikethamide by subcutaneous injection at intervals of three or four hours until the acute phase is passed is justifiable. Digitalis is of little or no value and a venesection, as it may accentuate the degree of shock, is better avoided. Anticoagulants *after* major emboli have occurred can be justified if an active phlebitis is still believed to be present in the veins of the calf or elsewhere.

Right ventricular failure, in a less acute form, also occurs as a result of chronic lung disease, such as emphysema or bronchitis. Broncho-spasm, paroxysms of coughing and particularly an acute exacerbation of the

bronchial infection, throw an increasing burden on the right side of the heart. Cardiac output is high in emphysema, except in the terminal stages of the cor pulmonale. It is therefore important to direct treatment primarily to the lungs and bronchi. Rest in bed at an even temperature, a sedative cough mixture (see p. 652) particularly at night, to reduce the frequency of the exhausting cough, and nursing with an efficient oxygen mask, even for several weeks at a time, are of first importance in successful treatment. The bronchial infection can often be overcome, at least temporarily, by penicillin aerosol inhalations and by sulphathiazole orally.

McMichael, who has made extensive investigations on this subject, considers that digitalis and venesections may be dangerous because they will produce a fall in right auricular pressure and cardiac output. On clinical grounds there is much to support his view, as remarkable benefit may be obtained by the administration of mercurials such as mersalyl intramuscularly on alternate days, without the corresponding use of digitalis. Even desperately ill patients, in right-sided failure, may rally and make substantial progress with the help of oxygen, mercury and sedatives. Digitalis is better avoided in these patients.

A. RAE GILCHRIST.

### ANGINAL HEART FAILURE

**Treatment of an Attack of Coronary Thrombosis.**—The *immediate treatment* of a case of coronary thrombosis consists in securing absolute rest in bed and the relief of pain by administration of morphia in full doses. Should the attack occur when the patient is at work or away from home, he should be given hypodermically  $\frac{1}{4}$  or  $\frac{1}{2}$  gr. (16 or 21 mg.) of morphia immediately on diagnosis, and should be sent home or to hospital or nursing home by car or ambulance. He must be assisted with his undressing, and should from the outset be debarred from all avoidable exertion. He must not rise to the toilet, and should not even sit up on the bed-pan. He will require to be lifted in bed for attention to bowels and for changing of linen, and even for change of position, so that the services of two strong nurses, trained or untrained, are desirable. It is unwise to allow a woman to undertake single-handed the nursing of a relative or other patient with this disorder, for the day and night nursing and the lifting involved impose too great a strain, and the temptation for the patient to ease the burden by doing things for himself is too great. It is wiser to send the patient to hospital at the outset than to move him some days later when his condition may be even more precarious.

The amount of morphia required to relieve pain is variable. The initial dose of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 21 mg.) should be repeated unhesitatingly in an hour should pain be unrelieved, and further repeated doses are likely to be required during the first twenty-four to forty-eight hours. For the later doses oral administration of the  $\frac{1}{4}$ -gr. (16 mg.) tablets at the hands of the attendant, under medical direction, is satisfactory. A limit is set to dosage only by the development of general toxic symptoms, for the drug exerts no deleterious effect on the heart. The relief of pain and the rest for mind, body and heart obtained by adequate doses render the drug invaluable.

**Other Treatment.**—Heparin and dicoumarol have been used in the treatment of cases of coronary thrombosis for some years, but there is as yet no

unanimity regarding their usefulness. The following remarks are based on the writer's personal experience, and might not command agreement from protagonists or antagonists of anticoagulant treatment.

It would seem that in the average case, in which occlusion of a coronary artery by clot has already occurred, anticoagulant therapy is needless, unless to prevent phlebothrombosis during the enforced recumbency of convalescence. There is, however, a group of cases in whom persistent or recurrent pain and prolonged shock indicate a spreading thrombosis (probably retrograde clotting above the original block, involving successive branches at higher levels) in which it is logical to attempt to limit the process. In cases where the electrocardiogram is typical of massive "through-and-through" involvement of the ventricular wall, there is considerable risk of intraventricular mural clot formation, with danger of subsequent embolism, and in these, too, anticoagulants may be useful. In both classes of case the danger to life is such that the risks of anticoagulant therapy are justifiable.

No one should embark on anticoagulant therapy unless he is prepared to keep his patient under close clinical observation for signs of overdosage (purpura, lowered capillary resistance, microscopic hæmaturia) and at the same time to carry out accurate estimations of blood coagulation time and/or prothrombin index. The known antidotes should be at hand (see p. 696).

The delayed and persistent action of dicoumarol, and its somewhat erratic nature, together with the difficulty in controlling its action should complications arise, have led the writer to abandon its use in coronary cases. Blood transfusion, the ultimate antidote if menaphthone fails, is hardly feasible in the subject of a massive myocardial infarction. Heparin on the other hand, though expensive and necessitating repeated intravenous injections, has so far given rise to no untoward reactions and has apparently been of value in several gravely ill patients. Its administration may be continued for several weeks in cases in whom intraventricular thrombosis is feared. For dosage see p. 695.

Nitrites and other vasodilators are useless in coronary thrombosis, and should not be administered, particularly as shock is usually marked and the blood pressure already greatly lowered. The administration of digitalis during the first week, and especially during the first few days, is inadvisable. The risk is due to the drug heightening the excitability of the ventricular muscle, and thereby favouring the onset of ventricular fibrillation, to which the coronary lesion predisposes. The use of digitalis in cases showing gross congestive failure is dealt with below. Quinidine sulphate, as a cardiac depressant, may lessen the risk of ventricular fibrillation, and in cases where there seems to be likelihood of this developing (cases with bursts of extrasystoles, or with ventricular paroxysmal tachycardia) it may be given in small doses of 3 gr. (0.18 gm.) thrice daily in a cachet.

Shock should be treated on symptomatic lines by warmth, etc., but such drugs as adrenaline, ephedrine or pituitary extract should not be given on account of their cardiac actions (for which see p. 683). Nikethamide and leptazol may be given, but should be reserved for desperate cases who appear in imminent danger of death. They are not required or desirable in the average case.

It is in the severely shocked patient that oxygen administration is of



conspicuous value. To be effective, the gas should be given in high concentration (say 6 to 7 litres/minute by B.L.B. mask, with all ports closed) continuously for many hours.

The diet of the patient during the first few days should be one demanding the minimum of effort in ingestion, and easily assimilated. The type of diet recommended for cases of severe congestive failure (see p. 634) will prove generally suitable.

Purgation should be avoided. The instillation of a few ounces of olive oil into the rectum, followed by a saline enema in the morning, is a safe and effective method of opening the bowels.

Various complications may arise during the first few days or weeks, and may demand treatment. Of these, progressive congestive failure should be treated along the usual lines. It may be necessary to give digitalis, especially if auricular fibrillation is present, but the drug should be given during the first few days only after a consideration of the risks run by its respective administration or omission. Diuretics such as the organic mercurials (mersalyl, neptal, novurit, etc.) or the purines (theobromine sodium salicylate, theocin sodium acetate) are of value, and venesection may afford relief in cases with great venous engorgement. Troublesome dyspnoea, interfering with sleep, can be treated by administration of aminophylline (0.1 gm.) by the mouth, or as a suppository per rectum (0.36 gm.) repeated two or three times a day. The development of progressive congestive failure after infarction is a very unfavourable sign, and the mortality of such cases is likely to be high despite treatment.

The occurrence of embolism is an ever-present risk, and cannot be foreseen. It is favoured by exertion on the part of the patient, but the risk cannot be eliminated entirely even by most careful nursing and attention. The treatment of cases where embolism has occurred is on symptomatic lines, and absolute rest is secured by morphia. From the nature of the cases surgical intervention is not generally practicable where arterial embolism of main limb vessels has occurred.

Recurrence of pain may occur at any time, and even slight persistent pain recurring over a period of days is disquieting. The treatment of such cases is renewed administration of opiates and prolongation of the period of rest in bed.

The actual duration of confinement to bed can be taken as six weeks in an average uncomplicated case. There are definite risks to life throughout the first few weeks after a coronary accident (recurrence, embolism, rupture of the softened area of muscle, failure), and these are increased by exertion. After six weeks or so these risks are greatly reduced, and a gradual return to activity can be permitted. The patient is first allowed to wash and feed himself, to sit up in bed for meals and later to rise to the toilet. Eventually, some eight weeks after the infarct, he should be up and walking about in his room for a few hours daily. The question of his future activities must then be considered.

Difficulty will often be experienced in persuading a patient to stay in bed for the prescribed period, particularly if, as often happens, he feels perfectly well a few days after the attack. The difficulty is naturally greatest in mild cases, or in those who have had no pain. It is advisable, however, to insist on a full period of recumbency even in cases with relatively minor symptoms. Explanation that the heart has been damaged, and that it

takes about six weeks to heal properly, will usually render the patient amenable to discipline. But one must be careful not to induce a state of undue apprehension of the hazards to be run, for much dispeace of mind may result, and more harm than good be done. The attitude of the doctor towards his patient is, in fact, worthy of some comment. The patient is generally aware from his own sensations of the seriousness of his condition. An attitude of unrelieved gloom on the part of the attending physician is not only inhuman but is not justifiable in view of the fact that two out of every three cases recover who survive long enough to be seen by a doctor. The risks to be run during convalescence must be kept in mind by the doctor, but must not be used as a bogey to frighten a patient into submission. And it should be realized that not the least of the patient's risks is that of developing an eventual cardiac neurosis which may be much more crippling than his organic lesion.

Cases who have suffered an attack of coronary thrombosis, whether or not residual effort angina persists, should in their after-care be treated on the same lines as the subjects of effort angina (see below).

**Treatment of Attacks of Angina of Effort.**—It is unusual for a patient to be seen by his doctor while actually suffering in an attack of effort angina. The attacks are of short duration and occur while the patient is about his daily business, and even if a medical man is summoned the pain is likely to have abated spontaneously before he reaches the patient. A patient whose pain has lasted without intermission for half an hour or more in spite of resting should probably be regarded as a case of coronary thrombosis and treated as such. Similarly, patients previously free from angina or suffering from attacks of moderate severity who suddenly develop attacks of great frequency on slight exertion should probably be regarded as cases of coronary occlusion and treated as such.

The patient who is habitually seized with precordial pain while walking generally realizes that continued effort aggravates his discomfort, and soon learns that he must stand still when pain comes on. In many cases this is sufficient to secure subsidence of the pain within a few minutes, and no medication is required. In more severe or resistant cases one or other of the quickly acting nitrites can usually be relied on to afford speedy relief, and the subjects of effort angina frequently carry such preparations in readiness for emergency use. The preparation most widely used is amyl nitrite, carried in small ampoules or "perles" containing 3 to 5 minims (0.18 to 0.3 c.c.). These are individually encased in fabric covers, permitting them to be broken in the fingers without fear of cuts from broken glass. The broken ampoule is held to the mouth and a few deep breaths taken with the mouth open. The action is speedy and relief from pain is frequently achieved. The vasodilator action produces flushing and often headache or giddiness, and the patient may hesitate to use the drug on that account, for such discomforts are to many harder to bear than a mild attack of pain. In severe attacks, of course, the benefits from nitrite far outweigh the unpleasant side-actions. Amyl nitrite fails to afford relief in a considerable number of cases, and the manner of its administration renders the user conspicuous in public. Dosage also is difficult to gauge. For these reasons the drug has been largely replaced by another, nitroglycerin, which is more reliable and, being taken orally, is less liable to cause embarrassment. Nitroglycerin is dispensed in tablets, frequently chocolate-coated, containing

the desired dose together with milk-sugar to make up a convenient weight. The dose required to abort an attack is variable in different cases, but it is convenient to prescribe the B.P. tablets of Tab. Glycerylis Trinitratis containing  $1\frac{1}{30}$  gr. (0.5 mg.), and to adjust the number of tablets taken to secure the appropriate dose. While relief may follow the taking of as little as  $\frac{1}{30}$  gr. (0.25 mg.),  $1\frac{1}{30}$  gr. (0.5 mg.) is usually required and sometimes  $\frac{1}{15}$  gr. (1 mg.) or even exceptionally  $\frac{1}{3}$  gr. (2 mg.) may be necessary. It is important to instruct the patient to chew and suck the tablets and not to swallow them, as absorption has been proved to be most rapid from the buccal mucous membrane. As this substance deteriorates when kept in contact with air for long periods, only small quantities of tablets should be prescribed at a time. Tablets stored in bulk should be kept in full bottles sealed with paraffin wax.

If nitrites are not available and the attack is severe and prolonged, alcohol, as whisky or brandy, may afford relief. But the use of alcohol even occasionally is not to be recommended, in view of the obvious danger of habit formation. Morphia likewise, which relieves the pain, is very undesirable in cases with chronic recurrent pain, from the risk of addiction.

After subsidence of the pain in an attack, many patients are able to resume walking or other activity where they left off, but should be warned that a slower pace than that which provoked the pain is to be adopted.

**The Management of Cases of Angina of Effort and of Convalescent Coronary Thrombosis.**—The treatment of actual attacks of pain should be looked upon as a very minor part of the treatment of a case of coronary disease. Reduction in the number of attacks is of vastly greater importance, and a great deal can be done by wise management to achieve this end. Much more will be achieved by regulation of the mode of life at work and at play, of habits regarding meals and the use of alcohol and tobacco, and by advice on other mundane matters than by the administration of drugs. It is a travesty of our therapeutic knowledge to diagnose a case as one of effort angina and to send him away merely with a box of amyl nitrite "perles" and instructions to take one when the pain is felt.

A large proportion of cases are of the overweight, thick-set type, and in these reduction in weight is probably our most potent therapeutic measure. The loss of one or two stones of superfluous weight greatly eases the burden imposed on the heart, and in our experience has repeatedly led to striking improvement in the exercise tolerance without the use of drugs. The sufferer from angina should be encouraged to attain a weight slightly under that which is average for the height, age and sex. This can be achieved by simple dietetic restrictions, provided the co-operation of the patient is secured. A further dietetic point hinges on the well-known tendency of attacks to occur when exercise is taken soon after a meal. Heavy meals are to be avoided, and a rest or short sleep after lunch or dinner may greatly reduce the frequency of attacks in some patients. Thyroid extract as a weight-reducing agent is not to be recommended in angina cases, in view of the increased cardiac load it imposes. Should its use be considered in an obstinate case the effect on the heart must be most carefully observed. It is wiser to discard it entirely in cases of cardiac pain.

The family physician, from his knowledge of the patient's habits and mode of life, is best qualified to instruct him as to what to do and what to avoid in his daily routine. A large proportion of cases occur in the active

type of business man around fifty years of age, and in these a careful consideration of the case will reveal what steps can be taken to reduce the demands that are made on the circulation. The avoidance of business worries, relegation of as much work as feasible to juniors, the giving up of committee work involving responsibility or the strain of meetings, etc., are all points requiring consideration. Physical effort can be reduced considerably by taking a little thought—securing offices or bedroom on the ground-floor where there is no lift; going late to the office and leaving early, and thereby avoiding the bustle and rush inevitable when the usual morning and evening train or bus is taken between suburb and city; cutting down the week-end golf from two strenuous days to a pleasant easygoing round, and so on. In cases occurring in men who are employed in heavy manual labour, or in vocations demanding physical effort (postmen, rent collectors, shopkeepers, etc.), it may be difficult to reduce exertion at work without jeopardizing the man's livelihood. In certain cases it may be necessary to change the occupation, where feasible, or to recommend retiral. Each case demands careful assessment, and great judgment in weighing the risk involved by continued work against the financial worry and hardship that will follow invalidism. Certain occupations should never be permitted to the subjects of severe angina, because of the risk not only to themselves but to others—e.g., drivers of locomotives, buses, etc.

In any case, whatever other measures are taken to spare the heart, it is always possible to arrange that the patient can have at least eight hours' sleep each night, with the additional rest of Saturday afternoon and Sunday in bed if required. At the outset of treatment in severe cases considerable betterment is frequently to be obtained by an initial period of two to three weeks' absolute rest in bed. The relief from attacks so attained may persist after return to activity, usually as an increase in the amount of work required to provoke an attack. Periodic spells of rest in bed are of value in many cases who otherwise have difficulty in securing enough rest.

The use of drugs is of minor importance, but nitroglycerin has recently been proved to be valuable in preventing, as well as in cutting short, attacks of pain. A patient who habitually gets pain on doing a specific act may prevent such attacks by taking  $\frac{1}{100}$  or  $\frac{1}{80}$  gr. (0.6 to 1.2 mg.) of nitroglycerin a few minutes before performing the exertion. Attacks produced regularly by climbing a flight of stairs may thus be prevented, or the strain of an important business meeting may be undertaken without discomfort. Many tablets can be taken daily over long periods with no apparent untoward results. For example, in cases of *angina decubitus* who are attacked by pain on turning in bed, or sitting up for a meal, or straining at stool, anything from ten to twenty tablets may be necessary to keep the patient free from pain throughout the day. The ambulant case who is using nitroglycerin to prevent attacks must be warned that they are intended to allow him to pursue his essential daily business at a very low level of energy expenditure, and are not to be taken with the object of allowing him to return to a more strenuous mode of life.

The widely advertised vasodilators of tissue origin (muscle and pancreatic extracts, etc.) are of little or no value in the treatment of angina; and should be avoided. Drugs of the caffeine group (theobromine and theophylline or theocin) have some reputation as coronary vasodilators, but their action is slight. A combination of 5 gr. (0.3 gm.) of theobromine and  $\frac{1}{2}$  gr.

(0.03 gm.) of phenobarbitone taken as a powder or tablet twice a day is sometimes useful; its action is probably mainly due to its sedative barbiturate content. A combination of theophylline and ethylene diamine, sold as aminophylline, is probably more efficient as a coronary vasodilator than the simple purines, though opinions differ as to its efficacy in practice. It is worthy of trial should nitrites fail, and can be given as a tablet by mouth in doses of 0.1 gm. or as a suppository (0.36 gm.), repeated in either case twice or thrice daily. Attempts have been made to treat anginal cases with nicotinic acid, which has a pronounced vasodilator effect, and with vitamin E (alphatocopherol). Neither of these drugs appear to have any advantage over nitroglycerin.

The place of surgery in the treatment of angina is discussed on p. 671.

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### DYSPNOEIC HEART FAILURE

#### *(Left Ventricular Failure)*

Occurring in acute forms this type of failure is usually an expression of left ventricular strain. The typical breathless attacks occur at night when the patient, about to fall off to sleep, awakens in distress, acutely uncomfortable, sits up in bed, struggles for air, and literally fights for his breath and for his life. The severer attacks of so-called cardiac asthma or paroxysmal nocturnal dyspnoea tend to pass on to acute pulmonary oedema, suffocation and death. The milder forms are frequently heralded by periodic breathing of the Cheyne-Stokes type.

The minor degrees of distress are eased to some extent by the resumption of the upright position, and as much fresh air as can be obtained from the wide open window. A support to the back and shoulders, often supplied by a table across the bed on which the arms may be rested, eases the burden, but the real relief comes from morphia, which should be given liberally as early as possible in the attack. A quarter of a grain (16 mg.) is usually sufficient to relieve the situation appreciably, but it may be repeated if necessary. As a rule, within a few minutes apprehension is decreased and the breathlessness checked in some measure. There is no completely adequate explanation for the mechanism of the onset of these attacks in which pulmonary congestion and broncho-spasm seem to play so large a part. The mode of recovery is equally mysterious. Morphia probably damps out abnormal reflexes and decreases the venous return to the heart by the mere reduction in muscular effort.

Digitalis takes second place in the treatment of the acute phases. That it is useful there is no question. To be effective it or an allied drug must be given in a large dose, preferably intravenously, but only then if the patient has not had one of the digitalis bodies in the previous ten days. For intravenous use digoxin (1 mg. or more for heavily built, plethoric individuals) is exceedingly useful. Digifoline is a proprietary preparation of digitalis bodies suitable for intravenous use in a dose ranging from 2 to 6 c.c. It has a clinical reputation in the treatment of this condition, but as with all digitalis bodies required urgently in large doses particular care must be taken to ensure that it may be administered with safety.

In from ten to twenty minutes after these drugs have been administered a definite easing of the respiratory embarrassment should be evident. The

patient should not be left unattended until it is obvious that the dyspnoea is well under control, that the cough has ceased and that sleep is bringing comfort. Unyielding cardiac asthma tends to advance a stage further to acute pulmonary oedema, a treacherous condition. Its onset is heralded by an irritating spasmodic cough, and later by the production of pink, frothy sputum at first scanty in amount and later becoming copious. In the earliest stages atropine,  $\frac{1}{100}$  gr. (0.6 mg.) hypodermically, repeated intravenously if necessary, is well worth using, but as a general rule with the appearance of the characteristic sputum a venesection will be required. This is best done by taking a scalpel and making a short longitudinal slit through the skin into an engorged vein at the bend of the elbow. The blood is allowed to spurt. After 10 to 15 oz. have been withdrawn, thus unloading the right side of the heart, a simple dressing and firm bandage applied with the arm elevated will rapidly arrest the bleeding.

There is often some hesitation in deciding under conditions of emergency such as these whether the use of adrenaline is warranted in the acute respiratory difficulties of left ventricular failure. Adrenaline is a powerful myocardial stimulant, and is contraindicated in both congestive and anginal failure. It increases cardiac work, but in small doses the element of broncho-spasm in the production of cardiac asthma may be eased by its use, and possibly the tendency to acute pulmonary oedema diminished. When it is judged that despite all his distress the patient is not passing into a state of collapse, when the pulse is of good volume, and particularly when the physical examination yields evidence of broncho-spasm in the form of sibilant rhonchi, inspiratory fixation of the chest wall and inspiratory retraction of the interspaces, then, contrary to general custom and belief, adrenaline may be used with benefit in small doses up to a maximum of 0.25 c.c. (4 minims) of the 1 : 1,000 solution. Just as adrenaline can relieve the distress of true bronchial asthma, so in dyspnoeic failure it may play a minor but helpful part, bronchial relaxation reducing the forced muscular efforts of breathing. Adrenaline, however, is in itself unlikely to abort an attack of cardiac asthma, as there are factors other than the mere broncho-spasm, but used in the small doses recommended in association with morphia or digitalis it does appear to be of value under certain conditions and in certain people.

The intravenous administration of 0.25 to 0.50 gm. of aminophylline (theophylline with ethylenediamine) has also been recommended, but hardly seems as effective as morphia. For this purpose it is obtainable in ampoules containing 0.25 gm. dissolved in 10 c.c. of sterilized distilled water. The injection must be made slowly at a rate not in excess of 2 c.c. per minute. It may be combined with intravenous digitalis medication. If, despite the measures already suggested, the attack continues, then the administration of oxygen should certainly be commenced by nasal catheter if a B.L.B. mask is not readily available.

Such a critical state as cardiac asthma or acute pulmonary oedema demands careful investigation for any exciting cause. Moreover, the recurrence of attacks is rendered less likely if the original be treated by a sufficiently long period of rest in bed. It is often the case that even by the following day the patient feels, though perhaps tired, almost fully restored to health. This is misleading, and absolute rest in bed for at least three weeks should be insisted upon. In cases attributable to an acute coronary

thrombosis a longer period of rest in bed is desirable. During the period of convalescence from the acute attack every endeavour should be made to ensure complete relaxation and adequate sleep. Simple dietetic measures may be commenced, particularly with a view to the reduction of excess weight, and as a rule it is worth while commencing maintenance courses of digitalis such as two  $1\frac{1}{2}$ -gr. (0.09 gm.) pills of the powdered leaf for five or six days at a time, depending on the patient's tolerance, omitting two to three days at the conclusion of each course as necessary. Despite such measures, bouts of nocturnal dyspnoea may continue, necessitating repeated emergency injections of morphia. To some extent this can often be countered by the administration of small repeated doses of opium during the afternoon or evening. Tincture of opium may be prescribed in a mixture in a strength of 5 to 10 minims (0.3 to 0.6 c.c.) to the drachm (3.6 c.c.), and of this 1 drachm (3.6 c.c.) taken at 2 P.M., 2 drachms (7.2 c.c.) at 4 or 6 P.M. and repeated at 8 or 10 P.M. may succeed in preventing the more acute disturbance through the night. Bedford has emphasized the value of parenteral mercurials in the prevention of dyspnoeic attacks. These drugs are as effective in the reduction of pulmonary congestion and oedema as in the peripheral variety for which they are more commonly used. Amino-phylline is capable of checking Cheyne-Stokes breathing when given intravenously, and is always worthy of trial. A quieter life and shorter hours of work are certainly desirable for many months after the acute phase of the illness is past. Digitalis usually requires to be continued indefinitely.

A. RAE GILCHRIST.

## DISORDERS OF RHYTHM AND INDICATIONS FOR THEIR TREATMENT

The presence of a cardiac arrhythmia is an indication for treatment only when the abnormal rhythm interferes with the efficiency of the heart's action. Sinus arrhythmia is a normal mechanism and requires no treatment. Occasional extra-systoles, or even short bouts of paroxysmal tachycardia, may occur in healthy hearts with no effect on cardiac efficiency. Minor degrees of heart block and auricular fibrillation with a slow ventricular rate are indications of cardiac damage, but do not in themselves necessarily limit the capacity for effort. In treating all arrhythmias attention should be directed primarily to the maintenance of ventricular efficiency, and in some auricular disorders, *e.g.*, fibrillation, this can be done without fundamental change in the abnormal rhythm.

### AURICULAR FIBRILLATION

Treatment has here to be considered under two heads: (a) That of the disordered ventricular action resulting from the auricular disturbance; and (b) that of the disturbance of the auricular contractions, the fibrillation *per se*. Of these, the former is usually by far the more important, and as in most cases it alone demands attention, it will be considered first.

When auricular fibrillation supervenes in a person whose heart is otherwise relatively healthy (as in cases of toxic goitre, many rheumatic cases and cases of paroxysmal fibrillation) the ventricles beat irregularly at a

high rate—over 120 and even as high as 180 per minute. The high rate, and the inefficiency conditioned by the total irregularity, usually determine the speedy onset of symptoms of congestive failure, and relief of those symptoms will follow reduction in the ventricular rate by suitable treatment. For this purpose bodies of the digitalis series are unrivalled.

On the other hand, patients whose heart muscle is extensively fibrosed (old arteriosclerotic and hypertensive cases) frequently have slow, though irregular, ventricular rates in the presence of auricular fibrillation, since a damaged *a-v* bundle cannot transmit as many impulses as a healthy bundle. In such cases auricular fibrillation may exist with an apex or pulse rate of 60 or 70 per minute; symptoms of failure due to high rate alone are absent, and digitalis loses its dramatic effect.

In a case of auricular fibrillation accompanied by tachycardia and congestive failure, the patient should be at rest in bed and nursed as a case of failure, with the customary restriction of diet and fluids, etc. Sleep is secured in many cases by simple measures, such as the barbiturates, but there need be no hesitation in giving morphia. This drug is relatively safe even in desperately ill patients, and often affords striking relief from sleeplessness due to dyspnoea. It is worthy of emphasis that the widespread mistrust of morphia in cardiac patients is baseless, and that the drug is of great value.

The patient should be fully digitalized without delay. The administration of digitalis is along the lines laid down on pp. 637-647. The choice of preparation and mode of administration will depend on the urgency of symptoms and the need for speedy action. Whatever method of administration is employed and whatever preparation is used the patient should be kept under observation during the period of digitalization. Palpation of the pulse is no real guide to the heart-rate, in view of the pulse deficit in such cases, and the apex-beat should be auscultated daily during this period. In hospitals the senior nurses should chart the apex-rate as ascertained by auscultation, as well as the pulse-rate.

The duration of digitalis treatment is generally for life. All cases on digitalis should be seen every few days after initial digitalization till the apex-rate has been stabilized, and thereafter should be examined at least once weekly for some time in order to establish exactly the suitable maintenance dose for the individual concerned. Patients who have been taking digitalis for months or years should occasionally be examined: instances are frequent in our experience where a patient has taken digitalis for long periods without adequate supervision, and where clinical examination reveals quite inadequate control of the heart-rate, with consequent limitation of the exercise tolerance or even congestive failure. Underdosage rather than overdosage is the rule in these neglected cases, and in general one may say that failures of digitalis in practice are frequent, and are almost always due to inadequate dosage. The only method of assessing dosage correctly is by frequent examination of the patient.

Vagal stimulation in animals fosters the induction of auricular fibrillation and prolongs the duration of such paroxysms. Digitalis as a vagal stimulant has a similar action, and in general the drug is best avoided in treating short recurring paroxysms in man. In a severe attack, however, the possibility of cardiac failure developing necessitates the use of digitalis to slow the ventricular rate, and curiously the administration of the drug



is frequently followed by reversion to normal rhythm. In a patient with auricular fibrillation of several hours' duration in whom distress is considerable and failure imminent, a milligram of digoxin may be given intravenously, often with dramatic result.

In cases with a low ventricular rate in the untreated state, digitalis is not indicated in the absence of congestive failure. Should failure be present the drug may be given with due caution lest untoward bradycardia result. Some benefit results in many cases, but the results are less likely to be dramatic than in the usual cases with high ventricular rate.

Treatment of the auricular disorder may be considered once the apex-rate is suitably controlled. It is well recognized that a proportion of cases of auricular fibrillation can be restored to normal rhythm by quinine derivatives, particularly quinidine sulphate. The prospect of success and the duration of the restored normal rhythm in any given case vary with a number of factors, and the use of the drug is not without risk; a full understanding of these points is essential before the treatment be embarked upon.

The drug is of most value in cases of auricular fibrillation of comparatively recent onset, without grave signs of muscle damage (enlargement, etc.) and particularly when the exciting cause of the arrhythmia has been traced and removed—for example, in cases of auricular fibrillation in hyperthyroid cases after operation. It is of some value, too, in cases of rheumatic origin of fairly recent onset, though here the prospects of lasting restoration of normal rhythm are less. It is of little value in cases of fibrillation of several or many years' duration, or in patients with grossly enlarged hearts and congestive failure. Should normal rhythm be restored in such cases, it is likely to be of short duration, and the benefits obtained are not commensurate with the definite risk involved in the treatment. Cases, too, with a previous history of embolism are unsuitable for quinidine, embolism from an auricular clot being a known risk of quinidine therapy, and the risk being increased by similar embolic accidents in the past.

In justice it must be admitted that, while from the foregoing it is evident that in our opinion quinidine is greatly limited in its value, in other centres the drug is much more freely used. It is argued that even a few additional weeks or months of normal rhythm is a considerable gain for a patient who is progressing toward the usual terminal phase of, say, mitral disease. Against this, one could quote cases of mitral disease who, when fibrillating with a well-controlled ventricular rate, were less dyspnoëic and able for more effort than when normal rhythm was present.

Should quinidine therapy be decided upon after due consideration, the drug should only be given after careful preliminary digitalis treatment. The ventricular rate should be well controlled, and congestive failure should have been abolished. The use of quinidine without these precautions is dangerous. A test dose of 0.2 gm. (3 gr.) quinidine sulphate in cachet is first given: some—a very few—patients show idiosyncrasy in the form of nausea, vomiting, tinnitus, or even collapse. Should no toxic symptoms develop, the drug is given in doses of 0.3 gm. (5 gr.) four-hourly throughout the twenty-four hours, with one dose omitted during the night to allow of eight hours' sleep; this dosage is kept up for several days or even a week. Electrocardiographic control is desirable, and careful clinical observation, preferably in hospital, essential. Should the fibrillation persist after this course it is repeated after an interval of a week, during which digitalization

is maintained. The proportion of cases that returns to normal rhythm varies with the type of case selected for treatment, but averages about one-third. In post-operative cases of thyrotoxicosis, practically all cases can be restored to normal rhythm—in fact, spontaneous reversion is common and may occur up to three weeks after thyroidectomy. The actual risk to life (from embolism, etc.) in well-selected cases though real, is low, and has probably been exaggerated.

In our opinion quinidine is a drug requiring considerable judgment in selection of cases, and skilled observation and care during its administration. It is a drug that for the treatment of auricular fibrillation has little place in general practice.

### AURICULAR FLUTTER

Unlike auricular fibrillation, the disordered auricular mechanism in this condition is influenced considerably by digitalis. In doses sufficient to produce ventricular slowing as in auricular fibrillation, this drug also causes conversion of auricular flutter to fibrillation in a considerable proportion of cases. The cessation of all digitalis medication in such a case, once fibrillation has developed, is followed in about one-third of the cases by return to normal rhythm; in another one-third of the cases the rhythm reverts to flutter, in the remaining one-third fibrillation persists as an established condition. In the former case, a second attempt with digitalis may succeed in establishing normal rhythm, or quinidine may be tried. In the latter case, the fibrillation is treated in the usual way, and again quinidine may be tried. In any case, the restoration of normal rhythm has the same prospects of duration as it has in cases of auricular fibrillation, and there is a similar risk of embolism.

In the treatment of a case with digitalis, the drug is given as in comparable cases of auricular fibrillation, and careful observation of the patient (especially his apex-rate) is essential. Whenever marked slowing occurs together with total irregularity at the apex, fibrillation may be assumed to have developed. This has occurred in our experience after a single intravenous dose of strophanthin, but it is more usual to induce it by oral administration of digitalis over a period of some days. Electrocardiographic control is useful, but hardly essential. When fibrillation supervenes, all digitalis is stopped for a few days and a return to normal rhythm awaited.

An alternative method is to use quinidine. After preliminary digitalization, to secure a slow ventricular rate and abolition of congestive failure, quinidine is given in similar dosage and method as for auricular fibrillation. Quinidine slows the rate of the auricular contractions, so that an auricular rate originally between 250 and 300 per minute falls gradually—it may be below 200 per minute. At this stage there is a danger that the ventricles may follow the full auricular rhythm (1 : 1 flutter) instead of responding to every second, third or fourth auricular cycle as at the beginning of treatment. Should this occur a dangerous ventricular tachycardia at 180 to 200 per minute may arise. This accident, however, is very rare. The slowing of the auricular rhythm to 200 or thereabouts is frequently followed by abrupt resumption of normal rhythm. Large doses of the drug are then stopped, and after twenty-four hours small doses of 3 gr. (0.18 gm.) once or twice a day are restarted and maintained for a few weeks.

It is our practice to use digitalis for flutter cases in the first instance. Quinidine is reserved for those which fail to respond to digitalis. In either case should normal rhythm be restored, its duration depends on the same factors as in cases of fibrillation treated with quinidine. Recurrence of flutter or fibrillation at an early date is likely in cases with grossly enlarged hearts or old-standing disorders of rhythm, and in those where a toxic factor (hyperthyroidism) is still operative.

### PAROXYSMAL TACHYCARDIA

**Supraventricular Paroxysmal Tachycardia** occurs frequently in people with no other discoverable abnormality in their cardiovascular systems, but also in various pathological conditions—rheumatic heart disease, toxic goitre, etc. In cases with an exciting cause, such as the last named, efforts should be made to remove it.

During attacks various measures may be employed to cut short a paroxysm. Any one of a number of procedures may result in the abrupt cessation of the attack, and many patients soon learn how to treat their own symptoms. The particular method which meets with success varies in individual cases, but frequently remains fairly constant for any particular individual. Bending the head low between the knees when seated on a chair, holding the breath, attempting forced inspiration or expiration with nose held and mouth closed, pressure over the abdomen, and vomiting, are all examples of procedures that patients may find useful in cutting short the attacks. The physician may stimulate the vagus reflexly and strongly by pressure over the carotid sinus on one or other side, and this frequently arrests the paroxysm. If this is attempted the patient should lie on a couch, and pressure with the finger-tips of one hand should be gently exercised over a point level with the upper border of the thyroid cartilage at the anterior border of the sterno-mastoid. The heart should be auscultated the while, and abrupt slowing or cessation of the sounds is the signal for immediate release of pressure. In some instances a first attempt is ineffective, but success may follow repeated attempts or stimulation of the sinus on the other side. Cases resistant to such sinus stimulation may yield to reflex vagal stimulation through the fifth nerve, from pressure on the eyeballs. Again recumbent, the patient is told to look down and close his eyes firmly. Pressure with the finger-tips on both eyeballs sufficient in degree to cause slight pain may produce cessation of the paroxysm. Ocular pressure, however, is unpleasant and painful, and is now seldom employed.

If all such attempts prove ineffectual, the induction of vomiting by emetics, or the production of nausea by subemetic doses of tinct. ipecac., may cut short the attack. A tight abdominal binder is often effective, especially in children.

In cases where these simple measures are ineffectual, attacks may sometimes be brought to an end by full digitalization. Quinidine sulphate is, however, more generally useful, and in doses of 0.3 gm. (5 gr.) three or four times a day by mouth, will usually bring the attack to an end. Hypodermic administration of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 21 mg.) morphia may secure needed rest for an anxious and exhausted patient.

With the development of symptoms and signs of congestive failure or of pain, indicating exhaustion of the heart muscle, the arrest of the paroxysm

becomes more urgent. Prompt arrest may be brought about by intravenous administration of quinine preparations, either quinine hydrochloride, or quinidine sulphate, 0.3 gm. (5 gr.) in 10 c.c. saline. These quinine preparations in high concentration are not without risk when given intravenously, and equally satisfactory results may be obtained by giving the drug in dilute solution as an intravenous drip (see below). Dramatic arrest may likewise be achieved by the intravenous injection of a drug of the parasympatho-mimetic group, *e.g.*, carbachol (B.P.). This is an ally of acetylcholine, a substance which physiological research has shown to be released at their terminations when parasympathetic nerves are stimulated, and which produces the characteristic parasympathetic effects on various organs. Acetylcholine is broken down too readily in the body to be of value in therapeutics, but other more stable esters of choline share some of its properties. Of these, acetyl- $\beta$ -methyl-choline (the chloride of which is marketed as Mecholin or Mecholyl) and carbaminoyl-choline (which is also known as Doryl or carbachol, B.P.) may be given intravenously to refractory cases of paroxysmal tachycardia. Fraser advocated Mecholin as preferable for this purpose. A usual dose is 25 mg. intravenously, though as much as 60 mg. may be required. The effect is produced within a few minutes, and abrupt return to normal rhythm occurs in a high percentage of cases. Carbachol is given in smaller doses (0.05 to 0.12 mg.), and is also effective. It has been noted, however, to produce auricular fibrillation in some cases. With either of these drugs other symptoms of excessive vagal stimulation may occur—nausea, vomiting or diarrhoea.

It should be remembered that the attacks tend to cease spontaneously and are generally of short duration—minutes or hours. Every day that passes in a resistant case renders the spontaneous arrest more likely to occur within a short time, and whatever medicament is being used will probably be given the credit of the cure.

**Ventricular Paroxysmal Tachycardia** is less common than the other form, and generally occurs in patients with grave myocardial disease, *e.g.*, after recent coronary infarction, etc. It may also occur from gross overdosage with digitalis. One form, however, is innocent and occurs in relation to exercise in apparently healthy people. In general, vagal stimulation is useless in treating these cases. Mecholyl, carbachol and allied drugs are of no value in this form of tachycardia and treatment by quinidine or digitalis is usually required. Quinidine is given as for supraventricular cases, and is very effective: the rate during the paroxysm may fall gradually under quinidine before normal rhythm is abruptly restored. Digitalis, though it can produce paroxysms of ventricular origin as a toxic effect, is paradoxically of value in arresting those of other origin. It is risky, however, in cases of recent coronary infarction, and in our experience inferior to quinidine. Treatment in cases of ventricular tachycardia with grave cardiac disease and gross failure is a more urgent matter than in the average case of supraventricular origin, and intravenous quinine hydrochloride (5 gr. or 0.3 gm. in 10 c.c. saline, given slowly) may be called for. In these cases also a quinidine sulphate drip given intravenously is of great value. Quinidine sulphate in a concentration of 50 gr. (3 gm.) in 500 c.c. of saline is given by slow intravenous infusion at a rate of 1 pint in 6 to 8 hours. Such a drip may be kept up for several hours. It is essential that a close watch be kept upon the heart-rate, and if possible electrocardiographic control is

advisable. Gradual slowing of the high ventricular rate occurs, with sudden reversion to normal rhythm in many cases after administration of from 5 to 20 gr. (0.3 to 1.2 gm.) of the drug. Once normal rhythm has been restored, quinidine sulphate by mouth should be continued as described below. Such drastic methods are, however, generally unsuitable for use in general practice, and are best reserved for hospital use with electrocardiographic control where practicable.

*Prevention of Attacks.*—Patients who have recently had an attack of paroxysmal tachycardia, or who are liable to repeated attacks, are generally benefited by a maintenance dose of 3 to 5 gr. (0.18 to 0.3 gm.) per day of quinidine sulphate over a period of weeks. Any obvious exciting factor (excess of tobacco or alcohol; thyrotoxicosis; septic foci in teeth or tonsils, etc.) should be attended to. Many cases are resistant and attacks recur at intervals over long periods of years without serious effects on the general health.

### HEART-BLOCK

The treatment of minor grades of heart-block is directed towards elimination of the cause. Little can be done by drugs to improve the conductivity of a damaged *a-v* bundle. Many cases are due to excessive dosage of digitalis, and clear up when the drug is withheld. Others are due to an intercurrent streptococcal throat infection, and subside as this clears up. Many occur in cases of active rheumatic carditis, and for these there is no specific treatment beyond the usual régime of rest and salicylate. A few cases are due to reflex inhibition of the bundle through vagal stimulation, and in these atropine in full doses of  $\frac{1}{8}$  to  $\frac{1}{3}$  gr. (1.2 to 2 mg.) intravenously, or full doses of tincture by mouth, may prove useful. In the minority of cases which are of syphilitic origin, potassium iodide may be of benefit, but it should be realized that actual gummata of the bundle are very rare. In that very large group of cases which occur as part of an ischæmia of heart muscle brought about through arterial degeneration, we have no specific drug of any proved value, and iodide has not in our hands deserved its time-honoured reputation. It is to be realized that simple prolongation of the *a-v* conduction time, or the occurrence of "dropped beats," is of no moment as regards the mechanical efficiency of the heart. Long-standing cases of 2:1 heart-block may have little or no limitation of effort, and demand no special treatment. It is to be emphasized, too, that digitalis is not advisable in cases of partial heart-block, as the drug may depress the bundle further and aggravate the condition.

Established complete heart-block is likewise not amenable to therapy. Such cases are usually due to scarring in the bundle region, which from the nature of things is irreparable. The management of such a case, however, is important: the patient should be warned to live within his reserve, and cautioned as to the risks involved by strenuous exertion, such as running upstairs, lifting heavy articles, etc. Unduly strenuous acts produce in such cases sudden syncopal attacks, since the heart is unable to accelerate to meet the demands for increased blood-flow to the tissues, and the cerebral circulation suffers accordingly.

High-grade heart-block in an unstable state is manifested clinically in many cases by recurrent classical Stokes-Adams attacks, to relieve which therapy may be of some value. The treatment of such cases is dealt with under Cardiac Syncope on p. 679.

### EXTRA-SYSTOLES

Extra-systoles occurring in young people with no other cardiovascular abnormality do not require treatment, and as a rule are very resistant to any medication. The patient should be reassured as to the innocent nature of his abnormality, should he be aware of it, and should not be allowed to permit the arrhythmia to interfere in any way with his normal activities. We are familiar with cases of persistent extra-systolic irregularity in healthy young athletes, and in men who, having had the disorder for many years, have reached the allotted span without mishap.

Patients who are greatly troubled by abnormal sensations due to extra-systoles may require a sedative, such as  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) of phenobarbitone. There is some evidence that the barbiturates may also diminish the frequency of extra-systoles in some cases.

Extra-systoles developing *de novo* in a patient demand careful overhaul to exclude organic cardiac disease, and also a search for possible exciting factors, of which examples are: heavy meals before retiring to bed; flatulence; tobacco in excess; septic foci in teeth or elsewhere; and digitalis overdosage.

Multiple extra-systoles may cause a pulse irregularity so great as to simulate auricular fibrillation. If one is certain that digitalis has not played a part in their genesis this drug in full doses is most useful in treating the condition. To be effective, digitalization must be thorough, and its administration does not differ from that in cases of auricular fibrillation. The continued administration of digitalis to a patient already intoxicated by it, is, of course, highly dangerous, and may lead to ventricular tachycardia and sudden death. Hence the necessity of making certain that digitalis is not responsible for the condition before starting treatment. Extra-systoles appearing in a patient receiving digitalis in any but the smallest doses should be assumed to be due to the drug till proved of other origin by their persistence for several days after cessation of digitalis therapy. Quinidine sulphate in doses of 3 to 5 gr. (0.18 to 0.3 gm.) twice or thrice daily is useful in some cases, and is relatively safer than digitalis in the first week after a coronary thrombosis.

Coupled rhythm, or *pulsus bigeminus*, though not always due to digitalis, very frequently is and should always be regarded as such in a new patient till proof is available that the drug has not been exhibited. Keeping this rule will avoid accidents from digitalis overdosage.

### SINO-AURICULAR BLOCK, NODAL RHYTHM, ETC.

There is no indication for medication in cases of sino-auricular block, or in the other rare disorders such as interference-dissociation. Some of these are prone to occur under digitalis therapy, and should such a cause be suspected the drug should be temporarily withheld.

## SURGERY IN THE TREATMENT OF CARDIAC DISEASE

For certain cardiac conditions relief may be obtained by surgical intervention on structures not anatomically connected with the heart itself, as, for instance, by sympathetic nerve section in cases of angina pectoris or hypertension, or by thyroidectomy in cases of heart disease caused by

thyrotoxicosis. The perfection of technique in surgery and in anæsthesia, particularly in respect of intra-thoracic operations, have, however, brought operations on the heart itself within the range of the possible. At first attacks were made on the stenosed orifice in cases of mitral stenosis, and the constricting bands were removed in some cases of chronic adhesive pericarditis. More recently ligation of the patent ductus arteriosus and an operation for relief of coarctation of the aorta have come into practice. The latest operation, which has yielded brilliant results in the hands of the pioneer Blalock, is designed to relieve the disability in congenital heart cases of the cyanosed group. Such operations, however, are emphatically beyond the scope of the average general surgeon, competent though he may be to deal in an emergency with such conditions as wounds of the muscle or hæmorrhage into the pericardium. Deliberate operations on the heart should be left for those who are specially interested in this field of surgery, in whose hands alone can such operations be undertaken with reasonable safety. No attempt will be made here to enter into details of technique. It is enough to indicate which types of case may be submitted to operation, with the prospects of relief which may be attained.

**Mitral Stenosis.**—Operations for relief of this lesion have been generally abandoned on account of the very high operative mortality and the unsatisfactory results in the few survivors.

**Congenital Heart Disease.**—Operations for the relief of Fallot's tetralogy, coarctation of the aorta and patent ductus arteriosus are discussed on p. 628.

**Pericardial Disease.**—Surgical operation is imperative in cases of purulent pericarditis, the establishment of free drainage by open or closed methods being as essential as in cases of pleural empyæma (see under Pericarditis).

In cases of chronic adhesive pericarditis operation may sometimes be usefully undertaken. In the type of case where the thickened pericardium is bound firmly to adjacent structures (ribs, sternum) a great deal of useless work is done by the heart-muscle at each systole. In such cases it suffices after reflection of the pectoral muscle and soft tissues to resect the ribs and divide adhesions to sternum, etc. Very striking improvement in the cardiac condition may result, and there are many records of patients with severe congestive failure who, after such operations, have returned to practically normal life. The operation on this type of case appears to be relatively simple, and to carry a low mortality. In the other type of case, where adhesions to outside structures are absent, but the two layers of pericardium are matted together, possibly extensively calcified, and where constricting bands around the orifices of the venæ cavæ are common, the operation is considerably more difficult and dangerous. The amount of interference required will vary from case to case, but a very extensive "decortication" of the heart may be necessary, stripping from the surface of the muscle the mass of scar tissue and calcium salts which impedes its movements. In many cases bands of scar tissue constrict the openings of the great veins, and these have to be divided. It is readily realized how great the technical difficulties may be, and in practice the surgeon must often rest content with partial operations. The results of such operations, though the initial mortality is rather high, are very satisfactory.

These operations on the pericardium offer such good prospects of relief with such a moderate mortality that all cases where adhesive constrictive pericardial disease has been diagnosed should be referred to a competent

surgeon for advice. This is especially desirable in cases with congestive failure which fail to respond to medical treatment.

**Operations for the Relief of Cardiac Pain.**—A great variety of operative procedures for the relief of pain in angina pectoris have been tried at one time or another, but those at present in use may be divided into the following groups: Operations on the sympathetic ganglia (resection or injection with alcohol); thyroidectomy; and operations for establishment of a collateral circulation. The last group, which was introduced shortly before the war, may be dismissed briefly. While other methods aim at merely symptomatic relief, operations of this group aim at revascularization of the ischæmic area of muscle. Various methods were employed, such as the use of grafts from the adjacent pectoral muscle or from the omentum. In each case the surface of the epicardium was stripped, and the graft (pectoral muscle or omentum) with its blood supply intact was stitched to the raw surface. The mortality was surprisingly low, and good results were claimed. The operation, however, never found general acceptance, and appears to have fallen into disuse. On *a priori* grounds operations of this type would seem most likely to yield lasting results in cases where progressive disease of the natural nutrient vessels has rendered the myocardium ischæmic.

Thyroidectomy in cases of angina pectoris has been widely employed, with at least initial success. The original operation was a complete excision of the gland, designed to produce myxedema, similar to that performed for the relief of congestive failure. Investigation has shown, however, that relief from pain is immediate, and is not dependent on the fall in basal metabolic rate which takes place in the weeks following operation. Some cases after operation have had their basal metabolic rate raised to normal by administration of thyroid extract, without return of pain. This paradox has led some authorities to suggest that the operation is effective because it involves the section of some nervous pain-pathway running over the anterior surface of the thyroid gland, and for which no other anatomical or clinical evidence exists. Those who believe this to be the case have modified the original operation to a seven-eighths partial thyroidectomy such as is performed in cases of thyrotoxicosis. The exact mode of action of the operation is therefore by no means clear, but there is no question that a considerable percentage of patients are markedly improved after operation. The operative mortality is low (3 per cent. in a series of sixty-seven cases in Boston hospitals, quoted by Means). The indications for operation will be discussed, together with those for sympathectomy, below.

It is well established that the sensory pain paths from the heart run in the sympathetic fibres and ganglia of the cervical and upper dorsal chain, principally on the left side, though occasionally in cases with right-sided pain the right chain appears to carry the sensation. These nervous paths may be interrupted by resection of the stellate and upper dorsal ganglia, or by injection of the ganglia with a sclerosing fluid (alcohol). Preference for one or other of these methods varies with individual surgeons; in skilled hands either method yields good results. The injection is relatively a minor procedure, performed under local anæsthesia, and very effective when skilfully performed, though on occasion fatal syncope has occurred during the injection. In some cases an obstinate intercostal neuritis results from implication of posterior roots in the resulting scars. Sympathectomy demands open operation, and, as a rule, general anæsthesia. The operative



mortality, however, is surprisingly low, and many of the possible pitfalls of the blind injection operation are avoided. In our experience a mild neuritis may follow the operation, but this has rarely been persistent or severe. It is most liable to occur where traction on the brachial plexus has occurred through difficulty in exposure of the ganglion, which is deep-seated and rather inaccessible. Horner's syndrome on the operated side is an inevitable and permanent sequel to the operation.

Cases of *angina decubitus* of extreme severity have been restored to a fair degree of activity and have been able to take up such duties as those of caretakers, etc. One case of angina of such severity that pain was induced by any exertion, however slight, so far improved as to return (without medical sanction!) to work underground in a coal-mine. Absolute relief from pain cannot be promised in any individual case, but is usually achieved. The objection raised by Mackenzie, that operation by relieving pain abolished the "red light" that signalled danger in over-exertion, appears to have been exaggerated. We have not met any instance where the abolition of pain has led to unfortunate results. The tenure of life in cases of coronary disease is notoriously uncertain, and an occasional unforeseen death in a case which has been operated upon should not rashly be attributed to the operation. We have noted further that many of the patients, though free from actual pain after operation, are still conscious of a vague sense of oppression on exertion, which indicates to them that the limit has been reached and acts as the warning against strenuous activity.

The question when to advise operation (thyroidectomy or sympathectomy) in a case of angina pectoris is one of considerable difficulty. The general attitude in this country is conservative, and in common with others we comparatively rarely send cases for surgical treatment. Probably only 4 or 5 per cent. of cases are suitable for operation by present-day standards. We advise it where pain is very severe and frequent, particularly in the type of case where, despite the maintenance of complete rest in bed, pain is relieved only by repeated administration of nitroglycerin. In such cases the relief obtained is generally so striking and untoward effects are so rare that operation will probably be resorted to more frequently in the future. Operation is also worthy of consideration in cases where pain severely limits exertion and where the heart, as judged by clinical, radiological and electrocardiographic examination, is relatively little damaged. Operation on this type of case is by comparison rare, and its advisability is a matter of debate.

**Surgical Treatment of Hypertension.**—The demonstration that ischæmia of one kidney might lead to severe and progressive hypertension in the experimental animal, and that removal of the injured organ led to regression of the hypertension, opened a new line of approach to hypertension in man. There is ample evidence that in patients in whom unilateral kidney disease is accompanied by high blood pressure, removal of the functionless and ischæmic kidney is followed by striking and lasting clinical improvement. Such cases constitute only a small percentage of hypertensives, but in a recent review Platt advises that in the investigation of all younger patients with high blood pressure, say under the age of forty-five years, and in all cases with symptoms suggestive of renal (non-nephritic) disorder, an intravenous pyelogram should be made with later retrograde pyelography if necessary. Platt also believes that such urological investigations should be done in all patients with no family history of hypertension. By such

methods the relatively rare cases of hypertension due to unilateral kidney disease (hydronephrosis, calculus, pyelonephritis) may be detected and advantage taken of the striking benefits from nephrectomy.

In the majority of patients no such lesion is present (essential and malignant hypertension). In these cases more or less extensive resection of the sympathetic nerves has been shown to afford some relief. The operations in use, of which there are several, vary in the extent of sympathetic resection, up to the extensive two-stage bilateral lumbo-dorsal sympathectomy of Smithwick. Great numbers of cases have been treated in the larger American clinics and operations have been done in many centres in this country. Reports as to their efficacy are conflicting, but there is certain evidence that not only symptomatic relief but regression of retinal and electrocardiographic changes may follow operation.

There is as yet no clear-cut body of opinion as to the indications for operations of this type. By common consent patients over fifty years are generally excluded, as are those with symptoms or signs of advanced irreparable damage to brain, heart, or kidney (hemiplegics, cases of angina or coronary thrombosis, renal failure). In the selection of patients the response of the blood pressure to sedation tests (sodium amytal narcosis) is of some value, those in whom little fall in pressure results from release of nervous tone being generally unfavourable. But the many exceptions render hard-and-fast rules unwise, since some patients with labile pressures fail to respond to operation and others with apparently fixed high pressures do very well. There is general agreement that cases of malignant hypertension in younger adults (up to forty-five or so) should be considered in relation to surgery, since relief of headache and other symptoms is often striking and on occasion papilloedema and cardiovascular signs regress after operation. Whether life is prolonged is debatable, but the patient may be spared intolerable distress. After operations of this type most patients develop a postural hypotension, which may prove troublesome for some time but is rarely a serious disability.

In summary, unilateral kidney disease is a rare cause of hypertension which should be sought for in all young hypertensives and in those with no family history of cardiovascular degenerative disease. When found at any age, removal of such a cause frequently leads to lasting benefit. In the majority of hypertensives, the "essential" group of the age fifty and upwards, operation on the sympathetic nerves or ganglia is probably inadvisable. In the younger age groups and particularly in the so-called malignant cases, sympathectomy should be considered, and the advice of a neurosurgeon sought after full clinical investigation of the case.

**Thyroidectomy for Congestive Heart Failure.**—Complete extirpation of the thyroid gland has been advocated as a measure in treatment of severe congestive failure, the rationale being that with a lowered basal metabolic rate the demands made on the heart to sustain a circulation adequate for the body at rest will be diminished. While some encouraging results were obtained, the general consensus of opinion now is that the operation has little place in the therapeutics of cardiac failure. The proportion of cases showing improvement, and the degree of betterment secured, seem inadequate to justify this major operation on critically ill patients. A less drastic and irrevocable means of attaining the same end is by the administration of thiouracil to such patients (see p. 425).

**Subtotal Thyroidectomy in Cases of Thyrotoxicosis.**—This subject is discussed fully in the section on Diseases of the Thyroid Gland, where the advantages and disadvantages of thiouracil and operative treatment are dealt with. Should operative treatment be considered necessary it is sufficient here to emphasize two points. First, that serious cardiac decompensation with auricular fibrillation is of itself no contraindication to operation in cases of thyrotoxicosis. Naturally, the cardiac failure should first be treated as a pre-operative measure, but the presence of severe cardiac decompensation, far from militating against operation, is an absolute indication that operation should be undertaken. No matter how late the case, how advanced the cardiac damage, there is no doubt that only harm can result from continued thyroid toxæmia. If the patient can be brought into a reasonable state, and the extreme congestion reduced, then operative removal of seven-eighths of the gland holds out a prospect of considerable amelioration, if not of cure, of the cardiac condition. Secondly, there is little doubt that many cases of thyrotoxic heart disease escape recognition. In cases of unexplained congestive failure in the middle-aged, especially with auricular fibrillation, and even in the absence of overt ocular or nervous signs of thyroid disease, the possibility of thyrotoxicosis as the cause of the myocardial failure should be kept in mind. Careful search for signs of hyperthyroidism such as loss of weight, sweating, glycosuria, etc., and a full examination of the thyroid gland may reveal the true cause of the heart symptoms. Again, hypertension and hyperthyroidism frequently coexist, and relief from one burden at least can be secured for the heart by judicious treatment. Paroxysmal auricular fibrillation in apparently healthy people should likewise suggest careful examination to rule out hyperthyroidism. I. G. W. HILL.

## THE CARDIAC NEUROSES

The conception of the heart as the organ of emotion dates from the earliest times. Avicenna, the ancient Arabian physician, who classified falling in love amongst the mental diseases, claimed that by a study of the pulse—its rate and rhythm—it was possible under particular circumstances to identify the person loved and to base on this knowledge an appropriate treatment. Such phrases as “broken-hearted” and “half-hearted” are remnants of the pre-Harveian notions of the circulation, notions which contain more than a nucleus of truth. There is every justification for the view that the circulatory system is a sensitive index of the individual's emotional state existing at the moment. In health, blood flow, both local and general, heart-rate and rhythm, blood pressure and vasomotor tone are all attuned by passing thoughts and ideas, even, it may be, of a most trifling nature. These reactions may well be intensified a hundredfold in the face of major emotional experiences. Sudden grief, joy, anger, shame, fear and such-like may each impose a burden on the circulatory system, with the production of acute symptoms ranging from perhaps no more than blushing or palpitation to giddiness, syncope, precordial discomfort, profound collapse or even sudden death. As a general rule the physiological reaction of the circulatory system to emotion is as short-lived as that experienced after physical exertion, but individuals vary as much in their mental balance, sensitivity to pain, whether it be bodily or mental anguish, and in their emotional make-up as in their general physique.

In this normal reaction of the heart to emotional stimuli we have the basis of an understanding of the altered mechanism of the cardiovascular system in those varied conditions which are roughly classified for descriptive purposes as functional circulatory states. Imaginary heart disease, neuro-circulatory asthenia (the effort syndrome), "angina innocens," and the cardiac neuroses form a group of different but related conditions associated with much distress, disability and economic incapacity. Often they are entities in themselves unrelated to any structural defect in the heart or circulation. This is not the place to review in detail the symptomatology of these various functional states, but as a general rule they are the products of conscious or unconscious emotional trends, anxiety for the future and lack of confidence in the present being firmly rooted ideas. It is equally true that a patient may constantly complain of disagreeable sensations identical with those produced by a passing emotion in a healthy individual without being aware at the moment of any exciting cause. In other words, an emotion can act without awareness in consciousness and from the point of view of treatment be less easy to detect and eradicate. The psychiatrist may divide such individuals into groups composed of anxiety states, obsessional neuroses and conversion hysterias. Quite commonly there may be a true psychosis, sometimes associated with an anatomical basis as in cerebral arteriosclerosis or in hypertension.

It is important to realize that not infrequently a functional nervous state consorts with an organic lesion, and treatment is therefore all the more complex. True angina pectoris is an outstanding example of an organic disease in which violent attacks may be induced by transient emotional disturbances recognized by the patient as anger, fear or worry. Similarly in rheumatic heart disease, long-continued anxiety, doubts and fears for the future may be the means of inducing a succession of symptoms mimicking serious disease. This is not uncommon in mitral stenosis—symptoms being partly organic, such as dyspnoea and fatigue, and partly functional as sub-mammary pain and giddiness. The knowledge, or even the suspicion, that the heart is the site of a morbid process is sufficient in the mind of most people to induce a train of symptoms based on fear, and culminating ultimately in an anxiety neurosis if unchecked at their beginnings. It is true that the mental reaction to doubt is apparently more intense in the case of the heart than in any other organ of the body. In the mind of the layman heart disease spells, if not sudden death, something incurable and irremediable. Only in the last stages of heart disease can it be said that there is a decreased response to emotion. It is remarkable that so often individuals in the final stages of congestive heart failure are naturally sanguine and retain, despite all their discomforts, an optimistic outlook. They are brave patients.

The term *imaginary heart disease* is best applied to those conditions which give rise to signs or symptoms simulating those of true organic disease, but in which the heart is not the seat of any structural defect. Innocent murmurs, precordial aches and simple syncopal attacks often suggest organic disease to the mind of the individual, a doubt which is intensified by an inadequate diagnosis and a faulty explanation of the mechanism of the production of the symptoms. It has been well said that the diagnosis of a "weak heart" or a "strained heart" under such circumstances reflects more on the doctor, who is weak and whose diagnosis is

strained, rather than on the patient's heart. These are terms to avoid. It is always a mistake to offer a half-hearted diagnosis, particularly when the integrity of the heart is in doubt, without a thorough and complete examination. Only then is it possible to assess the relevant facts. Such a diagnosis as a "weak" or "tired" heart may sow the seed of a protracted cardiac neurosis on very fertile ground. A hasty remark, a look or a nod, even an expression of doubt on the face of the examiner, may bring in its trail fears of crippling disability. With the universal knowledge regarding the vital function of the heart, symptoms are easily magnified, and unless checked in the most thorough way possible at the earliest opportunity, doubts accumulate and become more and more difficult to dispel.

Faced with such an individual the first step in treatment is the most thorough and careful examination possible, having first of all gained his confidence by encouraging the patient to give as full and as detailed an account of his symptoms as he may. The electrocardiograph and the X-ray have their therapeutic as well as their diagnostic uses. The examiner being satisfied in his own mind as to the nature of the disturbance, further treatment depends on winning the patient's co-operation by an intelligent discussion of the means whereby symptoms of a cardiac nature are produced. This is not always easy, nor is it always immediately fruitful in its results, as much must depend on the intelligence, education and co-operation of the patient. The physician must be prepared to justify his diagnosis and take as firm a stand as all the circumstances will permit. If the heart is judged sound, then it is a contradiction in terms to prohibit activities or to prescribe cardiac tonics.

In other instances it must be admitted that the basis of the *circulatory neurosis* is more deep-seated and repressed, so that only the special measures of the trained psychiatrist are likely to be fruitful. The family doctor, who is prepared to devote time and care to his patient, and has the opportunity to study him as an individual, knowing his upbringing, his personal traits and frailties, can do much to help and guide the neurotic. An earnest endeavour to analyse the particular situation and root out the source, origin and nature of the conflicts by frank discussion will accomplish far more in the long run than is to be attained by hasty and injudicious instructions to take a rest at a spa or a sea voyage in the tropics. The congregation of neurotics at health resorts often accentuates an individual's difficulties and widens the scope of his symptoms. Genuine emotional disturbances, reflected in circulatory symptoms, may result from all kinds of stresses and strains in modern civilization. Domestic worries, difficult economic circumstances, thwarted ambitions, private jealousies, sexual excesses, shameful dealings are all factors which, when frankly discussed and analysed, are often found to be in some measure correctable. When their true significance is appreciated, confidence gained and the facts faced in their true perspective, the individual may realize that his difficulties are often less embarrassing than might at first sight be imagined. In this way the family doctor can often ease the burden and reduce the emotional tension responsible for the individual's lack of adaptation. Circulatory symptoms can thus be eased and in time righted with perseverance, encouragement and reassurance. Simple explanations of the effects of pent-up emotions on the heart and circulation gradually come to be appreciated and understood as confidence is

regained. Drugs are usually not required, but insomnia must be corrected as adequate sleep is a first essential. Repeated examination of the heart and daily or weekly records of blood pressure are to be avoided, as thereby attention continues to be fixed on the circulation. Treatment is necessarily protracted, recovery is slow and only by perseverance is relapse prevented. Ross has shown that a large number of patients affected by the common neuroses, who are treated by a frank discussion of their symptoms, will become well and keep well. By demonstrating how their symptoms arise as emotional reactions, and by proving how they are retained because they are misinterpreted and by persuading the individual to appreciate their real value, much can be done to restore him to everyday activities. It is, in short, a method of restoration of confidence combined with the banishment of fear (Ross). Anxiety produces mental and physical exhaustion, and when this is adequately corrected by a short rest and the provision of sleep, it is right that these people should be encouraged to take as much exercise as they can endure. Constant encouragement, persuasion and a judicious optimism will rescue many from lives of incapacity. It is useless to offer to the confirmed neurotic the bald statement, even after a thorough examination, "Your heart is sound: go and forget about it." An encouraging clap on the back serves only to increase his discomfort. To him his symptoms are genuine and he has had no explanation for them. He distrusts more than ever. The neurosis is accentuated.

**The effort syndrome** or neurocirculatory asthenia is worthy of more detailed study in view of its intractable nature. Here, as in the simpler neuroses, it is our first endeavour to offer an explanation for the symptoms, reassuring as far as is justifiable and explaining the nature of the nervous and circulatory upset. The eradication of sepsis is important, but the most successful measures are those directed to simple outdoor exercise governed again by the patient's endurance, so that confidence is regained. The neurasthenic must be made to do more than he thinks he can. Light walks, gradually increasing in range and in rate for half an hour or so morning and afternoon, are of great benefit, associated later with a gentle outdoor occupation. These patients must be well fed and have ample hours of sleep. Drugs are of little or no value, and digitalis, as in all the neuroses, should not be prescribed, as by increasing the force of contractility it is liable to make the patient more aware of his heart. In any case, it does nothing to improve the circulation in health. The occurrence of this syndrome in the convalescent period after such acute illnesses as influenza, pneumonia or even tonsillitis, particularly in young adults, makes for special care in selecting an appropriate time for return to work. A hasty convalescence predisposes to this form of functional cardiac instability.

Treatment is rendered more complex when functional states and organic disease coexist. It requires a fine discrimination to steer a middle course, combining reassurance and encouragement with such physical limitations and drugs as the heart itself demands. In particular, in coronary disease associated with angina and hypertension, there is almost invariably an undercurrent of emotional tension, the correction of which can only be approached by a frank discussion regarding simple rules of behaviour, and the demonstration that fear is often unfounded. For this reason it is usually as unwise as it is unkind to offer the information to a patient that he suffers

from angina, though actually the prognosis in such a condition may run to ten or twenty years, for such a statement prejudices his progress and increases his anxiety. A simple explanation of his symptoms is all that an intelligent patient or his friends will desire.

## THE TREATMENT OF ACUTE CIRCULATORY FAILURE

In preceding sections attention has been chiefly directed to the treatment of those chronic forms of heart disease which ultimately lead to one or other of the common types of cardiac failure. Congestive, dyspnoëic and anginal failure are for the most part the end results of chronic degenerative lesions within the heart itself, and though each is liable to acute exacerbations these forms of chronic failure must be sharply differentiated from the various syndromes attributable to acute circulatory insufficiency. Heart failure and circulatory failure are not synonymous, for they differ in their exciting cause, mechanism of production and hence also in their rational treatment.

The term "acute circulatory failure" includes a wide variety of related conditions ranging from the mildest forms of simple syncope to the most profound degree of collapse, shock, coma and sudden death. The failure of the circulation in these states is more often attributable to a disordered regulation of the peripheral circulation than to any essential or intrinsic defect in the heart itself. A sudden decrease in the volume of blood in active circulation is the fundamental mechanism in the production of these circulatory syndromes. Thus it is that the symptoms associated with a profuse hæmorrhage differ only quantitatively from those of a simple syncopal attack. In the first instance blood is suddenly lost to the exterior, and the circulating blood volume is correspondingly reduced. In the second, the privation is none the less real as the amount of blood in active circulation is depleted by the stagnation of large quantities in the arterial and venous reservoirs. Peripheral dilatation as an acute disorganization of the vasomotor mechanism leads to pooling of the blood in stagnant areas with a consequent reduction in the venous return to the heart, a decreased output per beat, low peripheral pressure and more or less profound symptoms attributable to acute starvation of the central nervous system. Syncope, shock and collapse differ from each other only quantitatively (Weiss). Initially, various factors determine the onset and development of these syndromes, and treatment is determined by the correction of the exciting cause and the restoration of an adequate blood volume in *active* circulation to the vital centres.

### SIMPLE SYNCOPÉ

#### (*Vaso-vagal attacks*)

Cerebral anæmia in an acute form has many causes, and not the least frequent are those which operate through the nervous pathways. Disturbances of the autonomic nervous system leading to hypotension and transient cardiac inhibition are often reflex in origin, originating either from the highest cerebral centres or along the afferent pathways provided by the peripheral sensory nerves. Acute emotional distress, hypersensitivity of the carotid sinus, stimulation of the pleura or other sensory nerve endings



may each reflexly precipitate syncope. Hence, as Weiss has pointed out, attacks may be prevented by such different measures as the avoidance of emotional strain, the correction of psychological conflicts, the stripping of the coats of the carotid artery on the side of the more sensitive sinus, or by the adequate employment of local anæsthesia when surgical measures are contemplated. All these are methods of prevention appropriate for particular cases. In postural hypotension, which is often attributable to syphilis of the central nervous system, but which also occurs in a milder form in the severer anæmias, attempts to prevent the peculiar repeated seizures ought to be directed to the ætiological cause. When this is irremediable and permanent symptomatic relief may follow the use of  $\frac{1}{8}$  to  $\frac{1}{2}$  gr. (8 to 32 mg.) of ephedrine three or four times a day. Similarly mechanical support to the splanchnic area in the form of a suitably padded elastic belt and the development of increased muscular tone by a course of abdominal exercises are measures which may be employed to supplement drug therapy. The force of gravity constantly puts a burden upon the fine adjustments of the circulatory mechanism. Individuals prone to faint discover this fact for themselves. When attacks threaten they frequently lie down or adopt a sitting posture with the trunk flexed and the head thrown forward between the knees. Hot stuffy rooms, long hours in the erect posture without food or exposure to cold and damp are factors which predispose to syncope in susceptible persons.

The failure to maintain the erect posture which accompanies the act of fainting serves the purpose of rapidly correcting the cerebral anæmia by facilitating the return of blood to the heart and the vital centres. Treatment of the actual attack consists in loosening the clothing about the neck and chest and in placing the patient prone, or an even better effect may be obtained by the adoption of a modified Trendelenburg position. By laying the victim on his back and elevating the feet some inches from the ground, venous return is facilitated. Massage from the periphery towards the heart has a similar effect. Pronounced bradycardia and hypotension of reflex origin in severer cases may be corrected by the subcutaneous administration of 0.25 to 0.5 c.c. of adrenaline or  $\frac{1}{160}$  to  $\frac{1}{80}$  gr. (0.6 to 1.2 mg.) of atropine sulphate. When consciousness is regained alcohol has little to recommend it, but hot drinks of strong tea or coffee are often serviceable.

### CARDIAC SYNCOPE

Syncope of cardiac origin is attributable to an intrinsic disorder of the heart-beat. The symptoms may closely resemble a simple faint or may proceed to convulsive seizures and actual epileptiform attacks. The attack is usually transient and results from either extreme bradycardia, ventricular arrest or ventricular fibrillation on the one hand, or from an excessive ventricular rate as in the paroxysmal arrhythmias on the other. In either instance the symptoms are similar, and are due to cerebral anoxæmia. The prevention and treatment of the paroxysmal tachycardias, a potent cause of syncope in elderly people, have already been discussed (p. 666).

**Stokes-Adams seizures** are syncopal attacks associated with a defect, transient or permanent, in the conducting mechanism of the heart-beat. In the majority of instances they can be prevented by the regular administration of ephedrine hydrochloride in doses sufficient to increase by a few



beats per minute the slow idioventricular rate. For this purpose a dose of half a grain (0.03 gm.) of ephedrine by mouth in tablet form at either four or eight-hour intervals may be sufficient. Larger doses may cause over-stimulation and exhaustion of the ventricular centre. While ephedrine is the most reliable drug to use for this purpose it is not effective in every case, probably for the reason that the mechanism responsible for ventricular arrest varies in different individuals. Adrenaline, given by subcutaneous injection either as the B.P. preparation, or in oily solution which makes it slower in action, may be substituted for ephedrine, should the latter be ineffective. The proprietary preparation Adrenutol (adrenaline in oil) 1.0 to 2.0 c.c. by subcutaneous injection once or twice in 24 hours has the advantage of a more prolonged action. Barium chloride in doses of  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) by mouth in a mixture thrice daily has an experimental justification for its use in the treatment of the recurring syncopal attacks of heart-block in that it increases ventricular excitability, but clinical tests in patients liable to Stokes-Adams attacks have not fully substantiated this claim. Atropine is of little value, but may be tried if ephedrine, Adrenutol and barium fail.

Recovery from the actual Stokes-Adams attack usually occurs before any particular treatment can be prescribed. The ventricles resume their rhythm spontaneously. In the more severe attacks, as the circulation is in abeyance, subcutaneous or intravenous injections or inhalations are valueless, as the drugs are not transported to the heart. Therefore, in desperate cases recourse must be made to an intracardiac injection. Adrenaline is the remedy of choice. A fine needle about 3 in. long attached to a syringe charged with 0.25 c.c. adrenaline (1:1,000 solution) is inserted into the fourth left intercostal space about one finger-breadth from the sternal border. This site avoids the internal mammary artery and diminishes the likelihood of puncture of an underlying branch of a coronary artery or vein. The needle-point is inserted to a depth of 2 in. or more, and if the ventricular cavity is reached blood may be withdrawn into the syringe. The injection is then made, but actually it is of little consequence if the adrenaline is deposited either in the myocardium or within the cavity of the ventricle. The resumption of ventricular contractions is as a rule so immediate that it is questionable if the restoration of rhythm is attributable to the drug or to the local irritation of the needle in the myocardium. Ventricular systole is accompanied by an oscillation of the syringe and needle, and in a few seconds, if respiratory failure has not also ensued, by the rush of oxygenated blood through the skin of the face and neck. This method is life-saving, not merely in Stokes-Adams seizures, but also in the cardiac arrest of anaesthesia, electrocution and in anaphylactic shock. There is also every justification for its employment in asphyxia neonatorum, and in apparent death from the asphyxia of drowning. It must be obvious that the intracardiac injection of adrenaline is an emergency measure not without danger. Only the urgency of the situation justifies its use for which, fortunately, there is now ample experimental and clinical support.

It occasionally happens that Stokes-Adams seizures follow each other in rapid succession, the patient regaining consciousness only to lapse back again into coma every few minutes, perhaps twenty or thirty attacks occurring in the course of an hour. The milder seizures may amount to no more than a transient giddiness, but others proceed to profound coma and clonic

convulsions. Here, again, adrenaline is the drug to use. Within fifteen minutes of a subcutaneous injection successive seizures may be arrested. When these are severe and rapidly recurring, it may be judged advisable to give the drug intravenously, and for this purpose 0.5 c.c. of a 1 : 10,000 solution is ample. This dosage is easily accomplished by drawing 0.5 c.c. of the standard 1 : 1,000 solution into a syringe, and rediluting it by the addition of 4.5 c.c. normal sterile saline. After mixture 4.5 c.c. of the solution are discarded and the remaining 0.5 c.c. slowly injected into a vein at the elbow. Its total bulk may be augmented by further dilution, thus decreasing the risk of ventricular fibrillation.

Very occasionally Stokes-Adams seizures are due to this arrhythmia. Ventricular fibrillation is not necessarily a fatal condition, but if co-ordinate contraction of the ventricle is not quickly restored, death soon follows in a matter of minutes. The condition can only be recognized by the electrocardiograph, and when Stokes-Adams attacks are due to this abnormal mechanism it may well be justifiable to use quinidine sulphate in their prevention. Doses of 0.2 gm. in cachets three or four times a day are then worthy of trial.

### COLLAPSE AND SHOCK

These terms, which are virtually interchangeable, are employed to denote an advanced degree of acute circulatory insufficiency, more gradual in its onset, more protracted in its course and of much more serious significance than the simple syncope. There is no fundamental difference between "medical" collapse and "surgical" shock. The underlying mechanism, provoked by numerous agents, is similar in all three—syncope, collapse and shock. The amount of blood in *active* circulation is strikingly reduced.

Shock and collapse may occur relatively suddenly in the acute infections, notably lobar pneumonia; in acute sepsis as in peritonitis; in the course of acute intoxications, particularly delirium tremens; after spinal anæsthesia; as a result of mutilating trauma and profuse hæmorrhage; accompanying thrombosis and infarction, notably in the heart, lungs and brain; after an instrumental labour and in the post-operative period, particularly in middle-aged people with or without organic vascular disease. The peripheral circulation is disorganized as a result, it is believed, of dilatation of the smallest venules with either an associated dilatation or constriction of the arterioles. It is associated with capillary paresis and in the later stages with an alteration in the permeability of the walls of the finest vessels (Weiss). This has the important consequence of allowing the diffusion of plasma fluids into the adjacent tissue spaces. The circulating volume of blood is reduced as indicated by a rise in hæmoglobin percentage and a fall in blood pressure. Clinically the ashen-grey colour, the impaired mental acuity, the shallow respirations, the thready pulse, the cold perspiration and the falling arterial blood pressure make a fairly characteristic syndrome.

As regards treatment, posture is of the first importance. A horizontal or sitting posture may have to be maintained in certain instances, but whenever possible pillows should be withdrawn from beneath the head, and the foot of the bed raised on blocks to a height of 2 ft. or more. By this means alone the blood supply to the heart and brain is considerably facilitated. Cooling of the skin surface increases shock, and this must be countered by the application of a generous amount of warmth, either in the form

of numerous hot tins, or by the application of a "shock cage" in which heat is maintained by electric bulbs. Heat may be employed internally as well as externally by the provision of hot drinks either in the form of normal saline or as salty soup by the mouth, and by a hot solution of glucose, 5 per cent., in normal saline by the bowel if need be.

The correction of dehydration, relative or absolute, is particularly valuable in the acute circulatory failure of fever and in post-operative collapse, but considerable judgment is required regarding the parenteral administration of fluid in view of the danger of overloading the right side of the heart and of increasing the transudation of fluid through the weakened capillary walls, as occurs in the more advanced degrees of shock. If it is judged that the collapse is relatively mild, early in its onset and the heart fundamentally sound, then the restoration of a satisfactory circulatory volume can be brought about by a continuous intravenous saline drip. By this means 3,000 to 8,000 c.c. of fluid may be added to the circulation in the course of twenty-four hours or more. To the normal saline thus used various substances of value in the treatment of shock may be added; glucose, coramine and eucortone all may serve a useful purpose.

In traumatic shock, with oozing of serum into and around crushed and bruised tissues, with or without hæmorrhage to the exterior, recent clinical experiences re-emphasize the outstanding value of early and repeated transfusion of suitably typed blood in sufficient quantity to restore and maintain the blood pressure. A pint of blood or plasma in itself is seldom sufficient. By the use of the intravenous drip method, blood may be run into a vein at a rate of 100 to 200 c.c. per hour, and this can be maintained for twelve or twenty-four hours or longer, depending on the patient's progress and general reaction. In assessing the situation, repeated blood-pressure readings are of great value. A fall below 100 mm. is a danger-signal and usually indicates the necessity for further transfusion.

The demand for large quantities of blood at short notice has led to the establishment in recent years of blood "banks" from which stored and suitably typed blood can readily be obtained for transfusion purposes. From over-age stored blood the supernatant plasma has been removed and widely used with success in the restoration of the blood volume in shocked patients. Serum has also been employed. For ease of transport, stability and for the opportunity it affords of using higher concentrations of plasma, dried human serum has many advantages. The serum from all blood groups is pooled, concentrated and dried by special methods. The reconstituted solution prepared immediately before infusion by adding a suitable quantity of non-pyrogenic sterile distilled water to the dried serum powder, can be administered with safety to all blood groups without preliminary typing. This method has been used with great success in the treatment of shock.

With the intention of increasing the osmotic pressure within the vessels in order to re-attract fluid from the tissue spaces in the severer grades of shock, Best and his colleagues have suggested the employment of a solution of serum of four times the normal concentration in place of the usual solution of the serum powder or in place of whole-blood transfusion. This modification of the reconstituted serum for transfusion is still in the experimental stage. With concentrated solution the rate of transfusion should not exceed 50 c.c. in ten minutes. The method requires care and skilled observation, as the wisdom of introducing into the blood stream of a badly shocked

patient a highly viscous and concentrated fluid is open to doubt, though good results have already been obtained in a variety of conditions.

Various drugs have been used in the treatment of shock. Of these—at least on a theoretical basis—most justification can be claimed for the active principles of the suprarenal cortex. Suprarenal cortex extract, by correcting abnormal capillary and cellular permeability, is believed to regulate the volume of the circulating fluid within the vascular system. It is worthy of a more extended clinical trial in the treatment of shock and collapse than it has received to date. It may be given in doses of 2 c.c. every hour subcutaneously for an adult, or if added to a transfusion fluid, then 2 c.c. to each litre, if run at a rate of approximately 400 c.c. per hour, would appear to be adequate dosage. After two or three hours, if progress be made, the rate of flow should be reduced to half this quantity.

Anoxæmia has a detrimental effect on the central nervous system and aggravates all the features of shock. Oxygen therapy will be of value in those forms of anoxæmia in which œdema of the lung alveoli interferes with the absorption of oxygen. Pulmonary infarction and œdema, commonly associated with shock in the early stages, and the basal congestion which may rapidly follow an acute coronary thrombosis are examples of conditions in which oxygen therapy may be of value. In an emergency a nasal catheter is the best method of administration if a B.L.B. mask or an oxygen tent is not available.

Pain is a potent cause in the perpetuation of those reflexes disorganizing the peripheral circulation and promoting symptoms of shock. A fine discrimination is required to assess the appropriate dose of morphia to relieve the pain without augmenting the disordered peripheral circulation. It will be recalled that morphia itself in full doses acts through the parasympathetic system. As a general rule morphia is well tolerated in the early stages of shock and may be given in full doses if pain is at all severe. After some hours when the collapse is more advanced and the patient's general condition has deteriorated, then small doses are justifiable. It must be borne in mind that the detrimental effect of severe pain is to be dreaded more than the reaction of the peripheral circulation to the drug.

When the symptoms and signs suggest that the major factor in the production of the acute circulatory failure is a depression of the vasomotor centre, there are a number of useful drugs which may be employed with benefit. One of the best is strychnine, which is perhaps not so fashionable now as formerly. Clinical experience, particularly in the collapse of lobar pneumonia, indicates that this drug is of distinct benefit when given at hourly or even two-hourly intervals in doses of  $\frac{1}{30}$  gr. (2 mg.) or more. It increases the tone of the peripheral muscles, and may thus help the return of blood to the heart. It facilitates reflex action and there is evidence to suggest that it augments the tone of the vasomotor centres. It has no effect on the heart. There is no justification for the employment of digitalis in shock or collapse. The probability is that drugs of the digitalis group accentuate the degree of shock by inducing a further diminution in the volume-output of the heart. While the subcutaneous injection of camphor in oil in doses of 3 gr. (0.18 gm.) or more is ineffective owing to its slow absorption and insolubility, other synthetic organic compounds such as nikethamide (pyridine carbonate of diethylamide) or leptazol (pentamethylenetetrazol) appear to be useful and effective remedies when given parenterally in sufficient dosage.

The former is supplied in a 25 per cent. solution in 1 c.c. ampoules, and the latter in a 10 per cent. solution also in similar ampoules. In circulatory collapse of vasomotor origin either of these drugs may be administered intramuscularly in doses of 1 c.c. or more at hourly or two-hourly intervals. It is doubtful if they are really active by the mouth, and in circulatory collapse they can only be given intravenously with considerable caution and well diluted. In actual practice their intravenous use is perhaps limited to the collapse of barbiturate, morphine or carbon monoxide poisoning. They are probably less effective in the presence of organic heart disease, but may be used to counteract the minor degree of peripheral collapse inseparable from full and repeated morphine administration, *e.g.*, in the profound shock of a major coronary thrombosis.

On account of its cardiac stimulation and its power to constrict the peripheral arterioles, there is little justification for the use of adrenaline in profound collapse or shock, and pituitrin, for the reason that it decreases cardiac output, is not without danger. The fact is that the ideal drug for the treatment of peripheral circulatory failure has not yet been found. Weiss has suggested that a chemical substance which exerts a constricting effect solely on the venules will be of particular benefit, whereas a substance which simultaneously induces constriction of the arterioles as well may further impair the blood supply to the tissues. A drug with such selective properties has yet to be demonstrated, but the recent demonstration that a renin-like substance is set free in the blood stream during hæmorrhage and that it exerts a protective function in delaying the onset of collapse (Braun-Menendez) suggests that the ideal remedy for the correction of acute peripheral failure may be found in the complex renal pressor mechanism now the subject of intensive investigations. Until further clinical research has differentiated more sharply the different varieties of shock and collapse, and until more specific remedies become available, appropriate treatment must be based on rough-and-ready principles, the practitioner assessing the situation as best he may. Obviously all the methods outlined above are not desirable in every instance, but a selection may be made as the clinical state appears to indicate.

A. RAE GILCHRIST.

# DISEASES OF THE BLOOD VESSELS OF THE LIMBS AND THE EFFECTS OF COLD

## NORMAL PERIPHERAL BLOOD FLOW

**T**HE amount of blood which reaches the tissues of the limbs depends on the calibre of the arterial tree, which in turn depends on the tonus of the smooth musculature of the arterial blood vessels. Arterial tonus is controlled (1) partly by the activity of vasoconstrictor fibres belonging to the sympathetic nervous system, which are ultimately distributed to the vessels by way of the somatic nerves of the limbs, and (2) partly by the influence of chemical substances, either manufactured locally (products of muscular activity, which cause vasodilatation) or conveyed by the blood stream (adrenaline, which causes vasoconstriction). The arterial vessels may be grouped in two sets: those supplying the muscles, which are controlled partly by the mediation of chemical substances, and those supplying the skin and subcutaneous tissues, in the control of which the sympathetic nervous system plays much the most important part. The latter set of vessels takes part in the general vascular reactions which help to maintain the body at a constant temperature. When the temperature of the environment changes, that of the blood tends to follow the changes. The autonomic centres in the brain are sensitive to changes in the temperature of the blood which reaches them. When it is increased, the response is a generalized complete inhibition of vasoconstrictor tonus, so that a rapid flow of blood results, with a correspondingly increased loss of bodily heat. When it is decreased, generalized vasoconstriction of the superficial vessels is the response, which results in conservation of bodily heat. Adaptation to low environmental temperatures might be expected to be most difficult in the hands and feet, which provide the end-stages of the peripheral circulation, and which might not be warmly clad; the supply of heat to these parts by the circulation is greatly facilitated by the presence of special shunts (arteriolovenous anastomoses) between the subcutaneous arterioles and veins. When these anastomoses are relaxed by their controlling nervous mechanism, the resulting rapid increase in blood flow quickly warms the extremities.

For the development by the tissues of an adequate response to trauma and to bacterial infection, it is essential that both the peripheral vessels and the mechanisms for controlling the flow of blood in them should be normal.

## PATHOLOGICAL PROCESSES WHICH REDUCE BLOOD FLOW

The processes which reduce the amount of blood flowing through arterial vessels may be classified into two groups:—

**GROUP I.—AN ORGANIC CHANGE IS PRESENT FROM THE FIRST IN THE LUMEN OR WALL OF THE AFFECTED VESSELS.**

**A. Thickening of the wall of arteries:** In arteriosclerosis and syphilis.

**B. Embolism:** The embolus may (1) originate in the heart (auricular fibrillation, infarction, bacterial endocarditis), or (2) be detached from an atheromatous patch in an artery.

**C. Thrombosis:** (1) In arteriosclerosis (elderly patients of both sexes, especially diabetics); (2) in thrombo-angiitis obliterans (young or middle-aged males); (3) in syphilitic arteritis; (4) in polycythæmia vera, and leukæmia; (5) as a result of external pressure (tumours, cervical rib); (6) after debilitating diseases (pneumonia, typhoid); (7) without any apparent cause.

**GROUP II.—THE OBSTRUCTION TO BLOOD FLOW IS OFFERED BY SPASM OF THE VESSEL, AND ORGANIC CHANGES ARE (AT LEAST AT FIRST) ABSENT.**

**A.** As a result of trauma: A rare cause in large arteries; particularly after bullet wounds in their vicinity.

**B.** As a result of local hypersensitivity to cold: This is encountered in the small arteries of the hands and feet. Intermittent spasm of these vessels gives rise to the Raynaud phenomenon. The common type is the bilateral and symmetrical form met with in young women, and the phenomenon may also appear in the hands of those who work with vibrating tools. In both these types organic changes in the walls of the vessels may ultimately be superimposed on the original spasm. These tend to increase and to perpetuate the obstruction to blood flow.

**SUDDEN OBSTRUCTION OF LARGER ARTERIES**

When a main artery is obstructed by an embolus, the patient experiences numbness or pain in the limb and the skin becomes at first blanched and later cyanosed. Pulsation is absent beyond the site of lodgment of the clot. The temperature of the skin falls slowly to that of the environment. Loss of sensation and of power appear, and progress from the distal parts towards the proximal. The area involved in these changes depends on the availability of the collateral vessels, which are at first narrowed by reflex vasoconstriction. If they are inadequate, a sharp line of demarcation forms at a level which varies with that of the arterial block. Distal to this line the limb becomes gangrenous.

As soon as embolism is recognized the patient should be given 10,000 international units of heparin intravenously to prevent the spread of thrombosis from the site of lodgment of the embolus.

Since such an obstruction is likely to be permanent and progressive, the clot should be removed surgically (1) when it is aseptic, (2) when the general condition of the patient warrants such interference, and (3) when operation can be carried out within twenty-four hours. In cases unsuitable for operation, the development of a collateral circulation must be encouraged by warming the *unaffected* area of the body to about 45° C. (113° F.) by means of an electric cage, electric lamps, or hot-water bottles under sufficient coverings. When the area which will become gangrenous has been demarcated, it must be kept scrupulously clean and dry by the application of spirit followed by a sterile dusting powder.<sup>1</sup> If the patient survives, it may be amputated later.

<sup>1</sup> A suitable powder is a mixture of boric acid, 1 part; zinc oxide, 2 parts; and powdered starch, 3 parts.

### GRADUAL OBSTRUCTION OF THE ARTERIAL VESSELS

In practice this is a very common condition. As a rule, the morbid process affects both the superficial vessels and those of the muscles; but not infrequently the clinical features may direct attention particularly to one set, and they will be described from this aspect.

#### THE SUPERFICIAL VESSELS

The patient may complain:—

**Of Cold Feet.**—This is usually accompanied by changes in colour. Cyanosis is frequently present, and always indicates a slow circulation; if present in warm surroundings it must be regarded as abnormal. In the most severe cases the skin has a pale, waxy appearance. Blanching of the distal parts of the limb when it is elevated above the horizontal is frequently present, particularly in thrombo-angiitis obliterans. If the temperature of the environment is constant and the surface of the skin dry, surface temperature varies with the amount of subcutaneous blood flow; therefore the temperature of the skin provides an index of the efficiency of the superficial circulation. For accurate observations, special skin-thermometers of the thermo-electric type are necessary; in clinical examination a satisfactory estimation may be made by first palpating the skin of the suspected area with the dorsal surfaces of the middle phalanges of the fingers and then palpating the skin where the circulation is adequate (*e.g.*, feet, then forehead). Moreover, if both arms, or both legs, be exposed to a warm environment (23° C., 73° F.), then any difference in skin temperature is due to reduced blood flow on the less warm side.

**Of Nutritional Changes.**—The growth of the nails may be greatly retarded, and perspiration diminished or absent. Any breach of the epithelium heals very slowly or not at all, and there is a tendency for the development of indolent ulcers, especially on the heel and in the interdigital clefts of the toes. As the vascular occlusion progresses, areas of dry gangrene may develop, and this is often precipitated by careless nail-cutting or corn-paring (p. 689). Such an area may ultimately include a phalanx or an entire digit. In the final stages the foot, or the foot and leg, may become gangrenous. Both ulcerative and gangrenous processes are, as a rule, extremely painful.

#### THE DEEP AND SUPERFICIAL VESSELS

The patient may complain of *pain*. The cardinal symptom of inadequate blood flow to the muscles is *intermittent claudication*, a cramp-like pain in the calves and fronts of the legs which restricts exercise. This appears most rapidly if the patient walks uphill or fast, and in its most severe form it may force him to halt after he has walked as little as fifty yards. Claudication disappears if the patient rests.

Very inadequate blood flow in both superficial and muscular vessels is sometimes associated with severe pain which occurs during rest, especially at night; this is usually felt in the heel and/or in the sole of the foot.



In every case in which the history or physical signs are suggestive of vascular insufficiency, the pulses of the limbs must be carefully examined (Fig. 6); this should be done when the subject is warm, because pulsations are then maximal. This examination does not supply complete proof of absence of blood flow, because (1) vessels may pursue an abnormal course, (2) additional abnormal vessels may be present, (3) a partial obstruction proximally situated may diminish pulsation without seriously reducing blood flow (*cf.* coarctation of the aorta), and (4) although the walls of a vessel may be too rigid to pulsate it may be transmitting a fair quantity of blood.

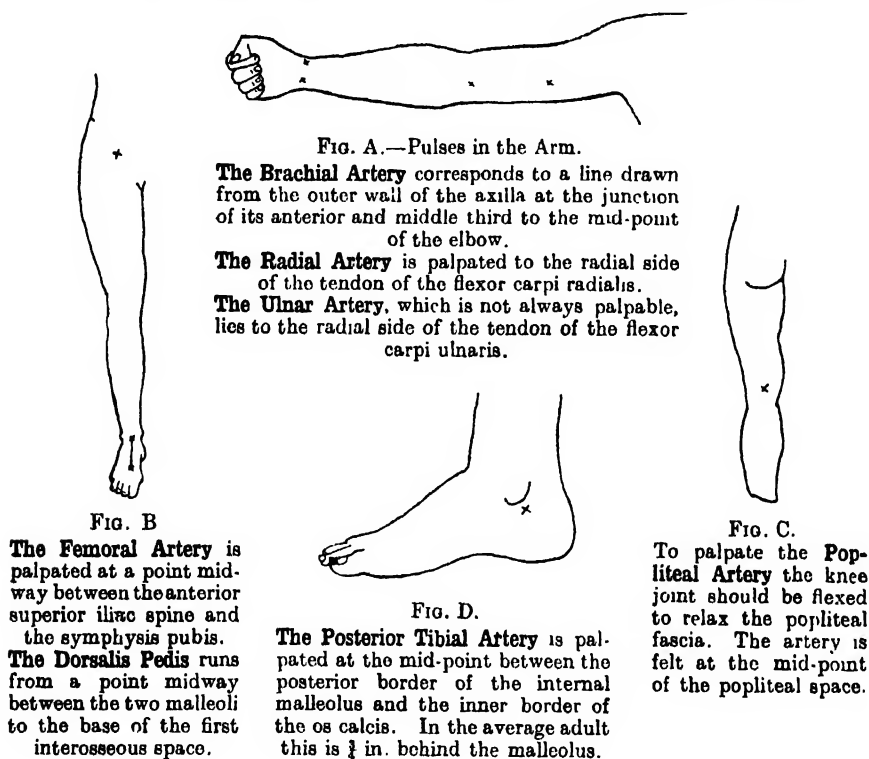


FIG. 6

The inexperienced observer may mistake the twitchings of adjacent tendons for arterial pulsation, particularly of the dorsalis pedis and posterior tibial arteries.

**General Treatment.**—The heavier the patient the greater the strain on his feet and legs; therefore any tendency to obesity must be corrected (see Treatment of Obesity, p. 383). Any glycosuria must be thoroughly treated because it may be of ætiological importance and because it predisposes to septic complications. Otherwise, since no individual food factor is known to be of ætiological significance there is no indication for interference with the patient's dietetic habits. Alcoholic beverages, in strict moderation, are harmless and, indeed, whisky at bedtime may, in virtue of its action as a mild vasodilator, be beneficial in such cases. In thromboangiitis obliterans smoking must be stopped completely. Rest pain is usually relieved by placing the legs in a dependent position, and the patient may be able to sleep in a chair or with the head of the bed raised. It is a wise plan

to arrange for the patient to have a succession of good nights at the beginning of treatment, by giving a mild hypnotic-analgesic such as soluble barbitone gr. v (0.3 gm.) with acetylsalicylic acid gr. v (0.3 gm.). Lack of sleep makes these old people (and often their households) irritable and unco-operative; after a good sleep they are different people, and the doctor will have the household with him. Clothing should be warm and not constricting. Woollen underclothes should reach the wrists and ankles, and bed socks must be worn. The patient should sleep between flannelette sheets or between blankets.

**Care of Threatened Areas.**—For the prevention or postponement of nutritional lesions the care of the threatened areas, especially of the feet, is of supreme importance. Patients should be given definite written or type-written instructions; these should be carefully explained to the patient and the importance of close attention to the carrying out of every detail strongly emphasized. It is quite true to point out that neglect of these instructions may mean the loss of a leg.

The feet and legs must be washed daily with *tepid* water and soap, dried carefully (especially between the toes) with a soft towel, and powdered with a dusting powder. Clothing must not compress them; thus socks should be woollen, seamless and of a good fit; boots and shoes must be roomy without being loose, without irregularities which might press on the soles of the feet (nails), and either soled with rubber or with an extra rubber sole. Prolonged standing is harmful; prolonged walking must be forbidden, the patient being instructed to stop within his known "claudication-distance." The feet must be protected from even the slightest trauma; thus nails should be cut straight and well away from the quick; corns should be pared only superficially, and never treated with destructive applications (e.g., salicylic acid). Those who can obtain the services of a skilled chiropodist should avail themselves of these, and the patient's doctor should be willing to act as chiropodist if required. The patient must avoid crowds, in which his feet may be trampled on with disastrous results. And finally, the feet and legs must never be exposed to cold, particularly to cold water (gangrene has followed incautious "paddling" in the sea).

**Care of Nutritional Lesions.**—The appearance of any breach of surface, however trifling, is of such potentially grave moment that the patient must rest in bed until healing has taken place. *Abrasions* should be gently cleansed with surgical spirit, and protected by a dry dressing of gauze or lint, held in position by a small strip of adhesive plaster (which must never completely encircle a digit) or by a light bandage. *Ulcers* about the toes or on the heel are as a rule very painful, especially when dressed; for this reason a suitable local application is an anæsthetic ointment.<sup>1</sup> If the ulcer is not painful, balsam of Peru or 4 per cent. thymol in liquid paraffin are alternative applications. *Small areas of dry gangrene*, e.g., up to a digit, must be kept aseptic and dry by the application of spirit two or three times a day, and are best exposed to the air, under a cage or box, without any dressing, in order to promote drying. Mechanical attempts to hasten the separation of the slough should never be made. The local application of heat is not good practice, for this raises the metabolic rate locally and increases the demand on an already deficient blood flow. Local removal, e.g., of a digit, should never be considered until a clear line of demarcation has formed; even then the

<sup>1</sup> Unguentum cocainæ; Benzocaine (B.P.).

decision to amputate locally is a matter of some judgment. In arteriosclerosis local removal may be considered if the tissues appear to be reacting well on the proximal side of the gangrenous toe; the incision should follow the line of demarcation, and the skin proximal to this must not be handled with forceps. The wound should be left open, or at most one loose stitch inserted. Local anæsthesia must not be employed to remove gangrenous digits, because it produces local tension; nitrous oxide, nitrous oxide and oxygen or intravenous pentothal are the anæsthetics of choice. Sometimes an angry reddening of the skin is seen about the base of a gangrenous digit, perhaps associated with lymph-angiitis of the foot and leg. This often heralds extension of the gangrenous process, but occasionally it is due to retention of pus by the hard skin of the gangrenous area; before more extensive measures are tried search should be made, particularly in the sole and interdigital clefts, and any small abscess drained by raising the dry black skin.

In diabetes the problems are a little different. If the patient is young, even a small area of gangrene, especially if it becomes infected, should be regarded as an urgent surgical condition of great gravity, and one requiring care in hospital<sup>1</sup>; whereas in older patients the gangrene is more often of the dry type and does not call for so urgent or so extensive treatment.

It must be emphasized again that if a small gangrenous area such as a digit is left to separate almost of itself, which is often the wisest plan, pain must be controlled, especially at night; but only as a last resort should morphine or one of its derivatives be employed for this purpose.

A major amputation is required (1) when gangrene is massive from the first, (2) when it involves more than the digits, (3) when it is associated with spreading septic infection, and (4) when it gives rise to intolerable pain. At least the relatives, and often the patient, should understand that the pathological process is bilateral and that the other leg may be affected at a later date.

**Measures Designed to Improve Blood Supply.**—1. *By Drugs.*—Numerous attempts have been made to improve blood flow by the administration of acetylcholine and its derivatives. The action of these substances is transitory, because they are rapidly destroyed in the body by a specific esterase. Their use is not recommended.

2. *By Operation.*—When the obstructive process is segmental, and parts of the arterial tree unaffected (a condition of affairs which may be found in thrombo-angiitis obliterans), an attempt may be made to improve the total blood flow in the limb by operation. The result of such an attempt depends on the availability of collateral channels, and/or their capacity to dilate. This can be determined by tests, which must be carried out in a hospital properly equipped to do so (see p. 692). If the test is satisfactory, sympathectomy may be performed to secure vasodilatation. Sympathectomy is seldom indicated in arteriosclerosis. In thrombo-angiitis obliterans operation should not be undertaken except after very careful preliminary study, and it must be emphasized that *claudication is rarely benefited* by sympathectomy, because the control of muscular vessels is predominantly chemical.

3. *By Buerger's Exercises.*—The patient lies on his back, in bed or on a couch. The leg is elevated to from 60 to 90 degrees above the horizontal and

<sup>1</sup> Since it is likely to be more of infective than of ischæmic type.

retained in this position by resting the heel on a support for from one-half to three minutes, the period required being that necessary to produce blanching. As soon as this is established the foot is allowed to hang over the edge of the bed until reactionary hyperæmia or rubor appears, and kept dependent for one minute longer; the total length of time in this position is from two to five minutes. The placing of the limb in these two successive positions constitutes one cycle, and each leg should be exercised in this way for six cycles three times a day. To be effective, the treatment must be faithfully carried out; if instituted early, its beneficial results are beyond doubt.

4. *By the Induction of Intermittent Reactive Hyperæmia.*—This is a most useful method of dilating the vessels in obstructive disease of arteriosclerotic origin. It is accomplished by the application of a pneumatic cuff to the thigh (or arm), which is alternately inflated to a pressure of 30 to 70 mm. of mercury for two minutes, and deflated for two minutes, the cycle being maintained by an apparatus driven from the domestic electric mains,<sup>1</sup> or by a cheaper but rather cumbersome apparatus regulated by the domestic water supply.<sup>2</sup> The distance which the patient can walk before claudication appears may steadily increase. In cases of this type from six to ten hours' treatment is necessary in each day; as patients readily accustom themselves to sleep while treatment is being applied, the hours of sleep can be utilized. After four to eight weeks of intensive treatment, each patient will discover the duration of his daily "maintenance" period of treatment for himself.

#### INTERMITTENT OBSTRUCTION OF ARTERIAL VESSELS

This group includes the cases in which the Raynaud phenomenon is the presenting physical finding. The essential feature of the commonest type, which is met with in young women, consists of attacks characterized by the sudden arrest of the inflow to the fingers, and possibly to a less extent to the toes. Usually an attack is precipitated by exposure to cold. The general physical findings are similar to those described on p. 686. At first nutritional changes are absent, but in severe cases of long standing, areas of superficial gangrene may occur at the tips of the fingers, as the result of the appearance of organic changes in the walls of the digital arteries.

**General Treatment.**—By far the most important principle in the treatment of this condition is avoidance of cold. Although local climatic conditions may make this difficult, at the least the patient must avoid cold in its most provocative form—cold water. Those who can afford it should winter in a warm, dry climate. Much can be done to reduce the frequency and severity of attacks by the adoption of proper clothing. The trunk should be warmly clad in order to minimize the amount of vasoconstrictor tonus imposed on the peripheral vessels. The limbs should be warmly clad from the root of the limb (clavicle, groin) to the hands and ankles; this keeps the blood warm on its way to the digits. For the hands, warm, loose-fitting gauntlet gloves are essential; for the feet, stout boots or shoes, allowing room for two pairs of stockings, and with additional rubber soles. The patient should sleep in a warm bed between flannelette sheets or blankets, with arms and hands under the bedclothes, so as to ensure at least eight hours each day of inhibition of vasoconstrictor tonus. Unfortunately for their comfort, most of

<sup>1</sup> The Chalmers-Edina Engineering Company, Leith.

<sup>2</sup> Messrs Baird & Tatlock (London).

these suggestions are as a rule rejected by young women, sometimes with scorn and often with hilarity.

When the condition follows the use of vibrating tools, the workman must find some other employment.

**Operative Treatment.**—When the patient has placed herself under the best possible conditions, and the attacks continue to be a source of economic or social disability, operation may be considered. This takes the form of division of the sympathetic vasoconstrictor fibres to the limb, and, if the point of section is properly chosen, worth-while vasodilatation of the superficial vessels follows. Of necessity, sweating is also abolished, and the dryness which results may be troublesome in the hands.<sup>1</sup> Before operation is undertaken it is essential that the capacity of the vessels to dilate be already demonstrated. This is a matter for the hospital clinic, where it is assessed by observing the rise in the surface temperature of the affected limbs when vasoconstrictor tonus is inhibited by heating a sufficient area of another part of the body. In practice the hands are most commonly tested; and the heat is applied by placing the feet and legs in water at 45° C. (113° F.). After a certain interval the temperature of the hands may rise to as high as 36° C. (97° F.), and must reach 30° C. (86° F.) before operation is justifiable.

Sympathectomy operations are not dangerous, and the period of disability is short (two or three weeks). No serious undesirable after-effects follow a well-planned operation.

### ERYTHRO-CYANOSIS

This is the term which Lewis employs to describe a condition which occurs almost exclusively in adolescent and young adult females. It is characterized by areas of defective circulation situated on the legs, particularly on the antero-lateral aspect, just above the external malleolus. Such areas are bluish-red in colour, and the skin is atrophic. The patients suffer in addition from cold feet, and burning pain is commonly felt when the blue areas are warmed. The condition is, as a rule, present only during the cold season, and disappears more or less completely during summer. In advanced cases ischæmic necrosis of the subcutaneous fat may occur and the skin may actually break, with the formation of indolent ulcers. Some oedema of the ankles and feet is commonly associated.

Patients should be advised to wear warm clothing, advice which, owing to the dictates of fashion, is rarely followed. In advanced cases, with severe ulceration recurring each winter, lumbar sympathectomy is indicated.

### THE EFFECTS OF COLD

**Frostbite.**—As its name implies, true frostbite occurs when the skin and possibly deeper structures actually freeze. Usually unclothed parts (fingers, ears, nose) are affected, but even well-shod feet may freeze after prolonged contact with ice or frozen ground. The affected area becomes dead white and hard, and as this transition may not be noticed by the patient, any companion with him must immediately call his attention to such an area.

*Preventive Measures* include the provision of suitable clothing, constant activity, the avoidance of direct contact with metallic objects and the minimum of exposure during micturition and defæcation. *Treatment* of small

<sup>1</sup> It may be minimized by the use of an emollient (cold cream) or glycerin.

areas is by covering them with a warm hand; larger areas (feet) may be placed inside the clothing of a companion, *e.g.*, in the axilla, or in cold water (under  $10^{\circ}\text{C.}$ ) if this is available. Massage and rubbing with snow are dangerous, because they lead to increased damage to the tissues. After thawing, the parts must be warmed gradually, and *never* by the direct application of heat. In severe cases, and when gangrene appears inevitable, the parts should be kept dry and sterilized by the application of an antiseptic such as proflavine 1 : 1,000. Blisters are best left unopened. At the first opportunity a prophylactic dose (3,000 units) of tetanus antitoxin should be given.

**Trench Foot.**—This may occur in soldiers who are occupying waterlogged trenches in cold weather. The essential cause is wet cold, and it may be accentuated by constricting clothing, physical exhaustion and inactivity. The feet become numb, and when boots are removed swell rapidly and become painful and discoloured. Its *prevention* is a matter of military administration. *Treatment* does not differ from that described for immersion foot in the next section.

**Immersion Foot.**—This condition is encountered in those (*e.g.*, shipwrecked seamen) whose feet and legs have been immersed for long periods in water below  $15^{\circ}\text{C.}$ ; the hands may also be affected. The parts become numb and swollen, and in more severe cases discoloured, blistered and even gangrenous. Later motor and sensory loss may ensue.

*Preventive Measures* are directed to the maintenance of activity, the avoidance of constricting clothing, and where possible the avoidance of prolonged immersion of the parts. Brisk rubbing is harmful. *Treatment* should begin as soon as possible after rescue. The patient should not be allowed to walk. The body is kept warm by blankets, but the feet must be kept cool and elevated to reduce swelling; in the often cramped conditions obtaining on rescuing ships, this may be attained by nursing the patient on his face, with the legs bent to right angles at the knees, supported in this position and left outside the bedclothes. On no account should the affected parts be warmed rapidly by the direct application of heat in any form. The local treatment of the parts is as for frostbite. Even in apparently unpromising cases, loss of tissue from gangrene is often minimal, and even minor amputation should be employed with the greatest conservatism. During recovery adequate relief from pain must be provided.

**Chilblains.**—A chilblain is an area in which the circulation has been disturbed by cold, often wet cold, in a susceptible individual; the smallest afferent vessels are contracted, the capillaries and smallest efferent vessels dilated. Treatment is largely preventive.

*General Measures.*—There is no specific diet for chilblains, but an adequate intake of calcium and vitamins, as supplied by a pint of milk and at least one helping of fresh fruit and green vegetables daily, should be ensured. Anæmia, if present, must be corrected and obvious sources of focal sepsis eradicated. Adequate exercise in the fresh air is of value in the maintenance of an active peripheral circulation.

*Drugs.*—There is no specific internal remedy. The very multiplicity of drugs which have been vaunted from time to time as specifics for the cure of chilblains is in itself an index of their comparative or complete inefficacy. Preparations of calcium, often combined with vitamin D, have been widely employed in treatment. There is no scientific basis for their use and it is very doubtful if they have any beneficial effect. Preparations of

the ovaries and the parathyroids and other polyglandular tablets have been much vaunted in medical advertisements. Given by mouth they are inert and there is no reason to believe that they are of the slightest value. Thyroid extract, however, may be administered with proper precautions (see p. 391) to obese patients with chilly extremities and is sometimes beneficial.

*Physical Measures.*—General irradiation with ultra-violet light appears to be helpful in some cases, particularly if given in the autumn prior to the onset of chilblains. When chilblains have developed, the circulation in the affected parts may be improved by the local application of ultra-violet rays or diathermy. Probably the most effective method of preventing chilblains consists in the rigid application of the methods already detailed (see p. 691) for keeping the extremities warm, and all other methods may fail if this aspect is neglected.

The distressing irritation of the chilblains may be minimized, if the skin is intact, by a paint containing 240 gr. (14.4 gm.) of menthol in an ounce (28.4 c.c.) of Tinct. Benzoin. Co.; if an ulcer is present, balsam of Peru may be applied under an occlusive non-constricting dressing.

## THROMBO-PHLEBITIS

In the treatment of venous thrombosis there has in recent years been a gradual abandoning of the previous policy of strict immobilization in the hope that the clot would become firmly adherent and that the venous blood would find alternative collateral channels.

**Thrombosis in Deep Veins of Calf.**—Diagnosis is of vital importance; it is based upon (1) a rise in pulse rate or temperature which cannot be accounted for on other grounds; (2) the detection of local tenderness in the calf on systematic palpation of the relaxed muscles; later, the tender area may be somewhat swollen and covered with shiny skin under which course distended subcutaneous veins; (3) the production of pain in the tender area on hyperextension of the ankle joint; and (4) possibly by venography. In such cases we agree with Bauer that anticoagulant therapy gives good results. An initial intravenous dose of 12,000 international units of heparin is given, and the same dose at 4-hourly intervals for the first 24 hours. On the following days three doses are given, the first two of 8,000 units, the evening dose of 12,000 units. When local signs and symptoms disappear, a supporting bandage is applied and the patient gets up and moves about, the drug is given for a day or two in doses of 8,000 units in the morning and evening, and finally only the evening dose is administered. When immobilization must be continued, the evening dose of heparin is given for 7 days longer, and all possible movements are carried out in bed. In suitable cases the patient leaves hospital about 3 days after getting up; a supporting bandage (Unna's paste bandage, viscopaste) must be worn for about 3 weeks.

**Thrombosis of Main Veins.**—The choice of active treatment lies between (1) anticoagulant therapy on the lines indicated in the preceding section and (2) surgical interruption of the main vein (usually the superficial femoral vein) on the cardiac side of the thrombus, combined with removal of the clot in early cases. Good results have been published by the advocates of each method; it is perhaps too early to be dogmatic, but our preference is for anticoagulant therapy except in those cases in which thrombosis has extended from a septic focus and the detached emboli have produced

pyæmic abscesses. In such cases sound surgical judgment is required in determining the level at which the venous system should be interrupted. In *phlegmasia alba dolens* the early institution of anticoagulant therapy is attended by gratifying results.

**Thrombosis in Varicose Veins.**—Beginning at some point in the long saphenous system, thrombosis may spread both proximally and distally to obliterate varying lengths of the long saphenous vein and its tributaries. The clinical features are local, there being little risk of pulmonary embolism. Conservative treatment consists in applying sorbo rubber, or orthopædic felt, over the thrombosed veins, and applying a supporting bandage (elastoplast or viscopaste) which should extend proximally above the proximal limit of the thrombus. The patient then resumes his normal activities. Although under this treatment the process resolves, there is a distinct tendency to recurrence, and the wisest plan is to advise the excision of the involved segments in an interval between attacks, the operation including ligation and division of the long saphenous vein at its junction with the femoral vein.

**Pulmonary Embolism and Infarction.**—In the majority of cases, the pathological process which may end in pulmonary embolism begins in the veins of the muscles of the calf. As a result of a number of contributory factors, of which the most important is stagnation of blood flow, a thrombus forms in one or more of these veins. This steadily increases in size until it reaches first the popliteal and then the femoral vein, when the course of the complication is determined by the fate of the clot: (1) the portion projecting into the main vein may be broken off by the more rapid stream and carried through the right heart to lodge as a pulmonary embolus; or (2) by growing in circumference as well as in length, the clot may block the lumen of the main vein (even, in rare cases, as high as the inferior vena cava) and give rise to gross œdema of the leg. From the upper less securely attached end of this column of clot a portion may be detached to form a pulmonary embolus. Except in debilitated patients, and those suffering from disease of the heart, stagnation of blood flow is usually a result of immobility after injuries or operations and in a previously healthy patient does not often lead to thrombosis until 3-7 days after immobilization.

**Prophylaxis.**—In debilitated patients and in previously healthy patients whose treatment requires immobilization (post-operative state, fractures), deep breathing exercises and active movements, particularly of the legs, should be insisted upon from the first. When operation is required in severely debilitated patients or in those with a previous history of thrombosis, anticoagulant therapy may be instituted without awaiting the onset of thrombosis.

When the embolus is large, death may follow with dramatic suddenness. In less extensive cases the clinical features vary from pleuritic pain followed in a few hours by hæmoptysis, to agonizing diffuse thoracic pain and dyspnœa which progress as the clot in the pulmonary arteries increases in size until death supervenes. Treatment, if possible at all, must be immediate. While successful cases of pulmonary embolectomy have been recorded, facilities for this highly specialized operation are not usually available, and we recommend the immediate institution of anticoagulant therapy, together with general measures. Heparin should at once be given in a dose of 12,000 international units intravenously, combined if pain be severe with morphine



$\frac{1}{8}$ - $\frac{1}{4}$  gr. (10-16 mg.), and continued at 4-hourly intervals in doses of 10,000 international units until the clinical features disappear, when the doses are "tapered off." The patient should be kept warm, and diffusible stimulants such as whisky, which have a vasodilator effect, are useful. As soon as possible the patient should be propped up to minimize the considerable risk of hypostatic congestion and broncho-pneumonia.

*Other Anticoagulants.*—Dicoumarin is an efficient anticoagulant, but has the disadvantage that its action is delayed for a period of 24-72 hours, and may be prolonged for a similar period after the last dose; moreover, its dosage must be controlled by frequent (preferably daily) estimations of prothrombin time, hence adequate hospital and laboratory facilities must be available. On the other hand, it is administered by mouth. Its use in the initial treatment of the urgent conditions dealt with above is not practicable, but when anticoagulant treatment is likely to be prolonged, certain workers claim excellent results from the simultaneous administration of dicoumarin and heparin, the latter being discontinued when the effects of the dicoumarin on prothrombin time become apparent.

The usual initial dose of dicoumarin is 200-300 mg. followed by daily doses of 100-200 mg., the exact daily dose—or its omission—being regulated by a study of the prothrombin time, which should be maintained at between 30 and 50 seconds (normal being taken as about 20 seconds).

*Complications of Anticoagulant Therapy.*—In heparin therapy hæmaturia of minor degree may occur, and rarely an anaphylactic reaction. The effect of heparin may be immediately neutralized by an intravenous injection of 5-10 c.c. of a 1 per cent. solution of protamine sulphate. Large or uncontrolled doses of dicoumarin may be followed by hæmorrhage which is occasionally dangerous to life. Should this occur, the drug must be stopped, and a transfusion, repeated if necessary, must be given, together with 50-200 mg. of vitamin K.

J. R. LEARMONTH.

# DISEASES OF THE NOSE, THROAT AND EAR

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## THE NOSE

### INTRODUCTION

**C**ONSIDERATION is given in this section to the treatment of the commoner affections of the nose and the nasal accessory air sinuses. Surgery plays its own part in connection with these affections, but as such it receives no present attention.

Similarly, lesions of the nose, throat and ear caused by syphilis, tuberculosis and malignant disease are not dealt with; they are more appropriately discussed in the sections set apart for that purpose.

### PHYSIOLOGY OF THE NOSE AND NASAL ACCESSORY SINUSES IN RELATION TO TREATMENT

Some knowledge of the physiology of the mucous membrane of the nose and that of the nasal accessory sinuses is essential to the intelligent treatment of diseases of these structures. The chief symptoms are, for the most part, the result of derangement of nasal physiology and, therefore, treatment is, in the main, an attempt to restore physiology to normal. The variation from normal may be in any one of the different elements of the nasal mechanism. Mucous membrane, of columnar ciliated type, is the structure upon which function is based. There are slight variations in the membrane in the different parts of the nose, as the more important functions are localized to certain areas. The mucous membrane is rich in glands which secrete the mucus which is essential to the life of the cilia. Under the basement layer of the epithelium is a connective tissue stroma, containing blood vessels and spaces which contain blood. These spaces form the erectile tissue of the nose, and are capable of engorgement with blood or of retraction, according to the functions of the nose in the supply of moisture and warm air to the lung. This erectile tissue is located chiefly in those parts of the nose upon which the air stream impinges—the anterior end of the inferior turbinate, its lower edge and the anterior end of the middle turbinate. This tissue is under the control of the sympathetic nervous system, and derangement of this is responsible for a great many symptoms of nasal disease which call for treatment. Mucus is secreted by the glands of the nose, and this has functions of its own. As has already been mentioned, it provides a medium in which the cilia of the columnar cells may live and work, and in order that they may carry out their function properly the mucus must be of the correct consistency. The mucus also has the function of protecting the membrane which lines the nose, and its absence or removal is immediately followed by changes in the mucous membrane and by symptoms of nasal discomfort. Particles of foreign material and bacteria inhaled

into the nose are caught in the mucus, and are eventually eliminated through the alimentary canal.

### PRINCIPLES OF TREATMENT

The main requirements for comfort in the nose and for normal physiology are adequate drainage, adequate aeration and ciliary activity; and it is towards the restoration of these that treatment, for the most part, is directed.

**Common Nasal Remedies.**—These consist of douches, sprays, drops, inhalations, powders and salves of various types. In accordance with the physiological principles which we have enunciated, no remedy which interferes with ciliary function is to be permitted. Therefore any remedy containing drugs in sufficient strength to paralyse or interfere with ciliary activity, as, for example, strong solutions of ephedrine, cocaine or irritants, must be avoided. Ointments or other applications which remain in a thick state within the nose will clog the mucous membrane, and thus prevent ciliary movement. Powders for the most part act as irritants and are not recommended. Douches, when used, must be isotonic, because water tends to paralyse ciliary activity. The main function of a nasal douche is to remove accumulated secretions which coat the mucous membrane and the nasal passages and prevent proper aeration and drainage. By removal of this accumulation the ciliary membrane is given an opportunity to recover, but it must be remembered that, as the function of mucus is to protect the membrane, the repeated and continued use of the nasal douche, by depriving the membrane of its protection, will tend to defeat its own end.

**Oily Sprays.**—These should be of light oil, of a non-clogging type and, if medicated, must not contain harmful concentrations of drugs.

**Drops.**—These are more effective than a spray from an atomizer, with which it is difficult to obtain an adequate and even spread of the solution throughout the nasal cavity. They have the merit that they are simpler to use, require less apparatus, and in many cases are all that is required for comfort. Oil should never be used as drops or sprays in young children or infants, owing to the danger of inhalation of the oil and the production of lung complications. Saline and ephedrine solution is used very frequently as a decongestive, in the form of drops or spray. The solution should be isotonic and should not contain more than 2 per cent. of ephedrine. To be most effective drops should be instilled in the supine position with the head extended.

**Inhalations.**—Inhalations of steam, medicated with menthol, camphor, eucalyptus, oil of pine or other substance, are frequently used in cases of nasal congestion. They are often of considerable benefit to those suffering from acute congestion of the nose, and the steam forms a convenient vehicle for the application of small quantities of soothing drugs to the mucous membrane. Prescriptions containing these remedies will be found in the Appendix (see p. 720).

**Other Forms of Treatment.**—Certain of these call for mention since, although outside the scope of medical treatment, they cannot be classified under a surgical heading. They are the galvano-cautery, the use of caustics and sclerosing solutions, ionization and various forms of radiation therapy. These have as their object the reduction of the bulk of the mucous membrane of the nose to provide aeration, or the correction of the sensitiveness of the mucous membrane to particular irritants.

### INJURIES OF THE NOSE

Treatment will vary according to the nature of the injury and the problems which it presents. Generally speaking, the conditions calling for attention fall roughly into three categories:—

1. Fractures.
2. Hæmatomata.
3. Epistaxis.

**Fractures and Hæmatomata of the Nose.**—These are largely surgical problems and their treatment will not be considered here.

**Epistaxis.**—In such cases two areas of the nose may require treatment. The first and commonest is Little's area. This is the name given to the part supporting the aggregation of veins at the anterior end of the nasal septum. The other area is the ethmoidal, in the upper part of the nose, which may also be the site of bleeding due to other conditions. The treatment of bleeding from the nose varies according to the area from which the bleeding is coming. In some instances it is unwise to treat the epistaxis immediately, because, if the loss is not severe or profuse, it may act as a relief to the patient as, for example, in cases of high blood pressure. On the other hand, when bleeding becomes profuse and troublesome to the patient, it will require to be controlled. If the bleeding must be stopped, there are two methods available. It may be controlled by pressure, that is by packing, or the actual bleeding point may be obliterated.

*The Control of Bleeding by Packing.*—If the nose is full of clot, an attempt should be made to clear it by douching. A solution of equal parts of peroxide of hydrogen and water, used cold, is recommended. After the nose has been douched, it should be packed lightly with gauze wrung out with 5 per cent. cocaine hydrochloride solution containing 5 minims (0.3 c.c.) of adrenaline to 1 drachm (3.6 c.c.) of cocaine hydrochloride solution. This packing should be left in for a few minutes and, when removed, the nose will be found to be comparatively insensitive and the work of packing the nose will be rendered very much less unpleasant for the patient. The doctor is able to carry out the packing more thoroughly when the mucous membrane reacts to the cocaine; also the mucous membrane will swell later, and by gripping the pack will increase its efficiency. The packing is carried out with 1-in. ribbon gauze soaked with a solution of hydrogen peroxide (10 volumes) or with a solution of snake venom (stypven, B. W. & Co.) or impregnated with iodoform. The floor of the nose is first packed. Six inches of the pack having been doubled, with a pair of angled forceps it is passed right back along the inferior meatus. From the floor of the nose the pack is built up towards the roof, being firmly pushed into all crevices of the nasal cavity. In the adult, at least one yard of gauze will be required on each side of the nose. In the vast majority of cases this is sufficient to control the bleeding, but if insufficient, a post-nasal plug will be required. To form the post-nasal plug, a piece of gauze is folded until it is of a size which will fit tightly into the nasopharynx of the patient. On an average, the gauze should be about the thickness of the thumb and perhaps not quite so long. It is tied round the middle with tape. A size 8 catheter is passed through the nose into the pharynx, where it is grasped by a pair of forceps and drawn out of the mouth. The end of the tape is tied to the

catheter, which is drawn back through the nose bringing the tape with it, thereby firmly anchoring the pack in the nasopharynx. The insertion of the pack, unless carried out with some degree of skill, is an unpleasant experience for the patient. To minimize the patient's discomfort, it is wise to cocaine the floor of the nose but also to spray the palate and the nasopharynx with a little cocaine. By depressing the tongue, the pack can be slipped into the back of the throat, from which position it can easily be pushed into the nasopharynx, this being assisted by traction on the tape. The tape should be anchored to the face by means of strapping. The packing is then carried out as detailed before, using the post-nasal pack as a base. In this way severe hæmorrhage can be controlled.

Control of hæmorrhage may also be accomplished by means of a pneumatic plug. A large-sized finger cot is tied to a fine gum-elastic catheter which is passed back into the nose. The bag can then be inflated, filling the nasal cavity. A plug or clamp closes the catheter and the bag remains inflated.

Nasal and post-nasal packs should not be left *in situ* for more than forty-eight hours without being changed, owing to the danger of pressure damage and infection, particularly of the middle ear via the Eustachian tube. This important point must on no account be disregarded.

*The Control of Epistaxis by Obliteration of the Bleeding-point.*—Cases in which the bleeding is from Little's area lend themselves to treatment by this method. The bleeding-point should first be identified and the front part of the nose packed with local anæsthetic, for example, cocaine hydrochloride solution (5 per cent.) with adrenaline. When this has been left in for a few minutes, the bleeding will be found in all probability to be very much less, and the bleeding veins will be seen to stand out clearly in the mucous membrane of the nose. Obliteration can be carried out either with the actual cautery or with a chromic acid bead. The electro-cautery is used at a dull red heat, and each vein in turn is obliterated with the point of the cautery, the cauterizing being made as superficial as possible consistent with the stoppage of the bleeding.

To control bleeding by chromic acid, a chromic bead must be made. To make this, a probe is heated gently in a spirit flame and some crystals of chromic acid are picked up on the point of the probe. The flame is then applied to the probe a short distance above the crystals. After a moment or two the crystals melt, and run down to form a drop on the point of the probe. As soon as the crystals melt, the probe is withdrawn from the flame and, by rotating the probe gently, a drop adheres to the point of the probe until it cools. The point of cooling is marked by the change from a bright, shining, black bead to one of a dull coke-like appearance. The bead is then used in a similar fashion to the cautery, but it must be used sparingly and the excess of acid must be wiped away immediately after each application or must be neutralized with alkali.

#### GENERAL TREATMENT

Brisk nasal hæmorrhage is frequently an alarming experience for a patient, and it is very often wise before commencing treatment to give the patient an injection of morphia or other sedative. This will help in many cases to control the bleeding by keeping the patient quiet, and will

make subsequent manipulations very much easier for the doctor. It is not proposed to deal here with nasal hæmorrhage as the result of blood disease or other systemic conditions, as the treatment of epistaxis in these cases, apart from the purely local measures detailed above, belongs properly to the sections in which these diseases are found.

### AFFECTIONS OF THE NOSE

**Rhinitis.**—*Acute Rhinitis.* (See Coryza, p. 725.)

*Purulent Rhinitis.*—This form of infection is most frequently seen in conjunction with the exanthemata, and signifies a virulent infection of the mucous membrane of the nose. Locally, it is treated with douches and ordinary cleanliness in conjunction with the general treatment of the diseases during the course of which the condition occurs. These may include the administration of penicillin.

*Membranous Rhinitis.*—As this condition is most frequently due to the Klebs Löffler bacillus, the treatment is the same as in cases of diphtheria. Other forms of membranous rhinitis are found in patients suffering from marked debility, and in such cases they may be treated with mild alkaline douches, instillations of drops, such as mild silver protein (B.P.C.) (10 per cent.), silver protein (B.P.) (10 per cent.), and other non-irritant applications. (For prescriptions, see Appendix, p. 720.)

*Chronic Rhinitis.*—The treatment of chronic rhinitis depends to a considerable extent upon the stage to which the chronic condition has advanced. In the earliest stage the return of comfort to the patient depends upon the restoration of ciliary action and, as this is prevented by the want of proper aeration in the nose and the clogging of the mucous membrane with thickened secretions, treatment should be directed towards the relief of this condition, and alkaline douches are indicated. Inhalations of menthol will help to decongest the mucous membrane. Menthol must not be used, however, in very young children. A spray containing 0.5 to 1 per cent. of ephedrine in normal saline or liquid paraffin is useful for a short period, but should not be prescribed for prolonged use.

Where the rhinitis has progressed to the hypertrophic form, which means the laying down of fibrous tissue within the mucous membrane, then treatment must be directed in the first place to the removal of the non-functioning fibrous mucous membrane, and this, therefore, will entail operative procedures.

*Atrophic Rhinitis.*—In atrophic rhinitis there is such extensive change in the mucous membrane, and sometimes in the underlying tissues and structures, that treatment offers but little hope of restoration of function. Treatment therefore resolves itself into the problem of providing the maximum comfort for the patient under the circumstances. This means that the accumulation of secretions has to be removed, because, owing to the lack of ciliary action, crusts form within the nasal cavity and the patient suffers from chronic obstruction of the nose. A certain amount can be done to moisten the thin and dry nasal mucous membrane, but, except in the *earliest stages*, the condition cannot be cured and even then can only be checked.

The removal of the crusts is best carried out by means of douching, with or without the preliminary softening of the crusts within the nose. If the

crusting is heavy, the patient should be instructed on rising in the morning to plug both nostrils with cotton-wool to moisten the crusts. After about half an hour, he should douche the nose with a weak saline solution, *e.g.*, 1 teaspoonful of salt to a pint of warm water. Where the crusting is not heavy and the condition is in the earlier stages, the nose should be douched with mild alkaline solution (see Appendix, p. 720).

The nose can be douched morning and night; but, if douching once daily is sufficient, cleansing should be confined to this one occasion. Excessive douching is apt to lead to irritation and further discomfort. After douching, the nose should be sprayed with an oily solution. A light oil is best for this purpose and may contain some essential oil to render the odour pleasant. This helps to protect the mucous membrane, and also tends to delay the formation of crusts.

Another form of treatment consists in spraying the nasal cavity with œstradiol in oil (0.5 c.c. of a solution containing 5 mg. per c.c. is sprayed into each nostril). This should be undertaken daily at first, and as improvement becomes evident by the diminution of crust formation and the disappearance of odour, treatment can be carried out on alternate days and the period lengthened gradually according to progress, until the spray is being used once weekly or once in a fortnight. In favourable cases it can be omitted altogether. It is essential for the success of this treatment that cleansing of the nasal mucous membrane should be meticulously carried out. This is done by douching, as described above, and if necessary in the earlier stages, by picking out the crusts under direct vision.

**Ozæna.**—This affection is sometimes described as a separate entity, but it closely resembles atrophic rhinitis, the only additional feature requiring attention being the fœtor which is characteristic. Treatment follows the lines indicated above.

**Nasal Polypi.**—The treatment of nasal polypi is symptomatic only, in so far as this section is concerned. A careful search must first be made for the underlying cause, and the method adopted will depend upon what is discovered. Treatment may be instituted, for example, on account of an allergic basis for the polypus formation, or investigation may indicate an underlying affection of the sinuses. Local treatment of the polypi consists in their removal by forceps and wire snare. Occasionally, it is found that polypi disappear spontaneously, but expectant treatment should never be adopted in the hope that this may occur.

**Syphilis and Tuberculosis.**—These conditions are fully dealt with elsewhere and need not be mentioned here (see pp. 210, 110).

**Nasal Allergy.**—The question of allergy is also considered on p. 764 and antihistamine drugs (see p. 96) may be of great value. Local treatment, however, may be called for in the nose. Ephedrine is the most useful drug in such cases. Ephedrine is applied preferably in the form of drops in normal saline solution (0.5 or 1 per cent.).

Zinc ionization will in many cases give complete comfort to the sufferers from nasal allergy. It has been used to a great extent in cases of specific nasal allergy, as, for example, hay fever, but is also of value in the non-specific types of sensitivity, such as sensitivity to dust or to temperature change.

**Foreign Bodies in the Nose.**—Removal is the only treatment for foreign bodies in the nose. If a foreign body is close to the nasal vestibule anteriorly,

it is usually easily removed, provided a suitable pair of forceps is at hand and adequate assistance is available to control the patient. If the patient is old enough to co-operate, it will be found of considerable advantage to shrink the nasal mucosa with 10 per cent. solution of cocaine containing adrenaline (1:1,000)—5 drops of adrenaline to the ounce of cocaine solution. This will facilitate manipulation and, by the shrinkage of the mucous membrane, will render the removal of the foreign body a comparatively simple matter. In the case of a small child, the patient must be controlled by another person, preferably not the mother, and it is useless to attempt the removal of the foreign body unless the assistant is capable of holding the child perfectly still. It may be necessary, in cases of doubt, to give an anæsthetic in order to make a complete examination of the nasal cavity. An anæsthetic in such cases should never be given without adequate preparation, for the child is frequently frightened and resistive, and, as such, may make an extremely bad subject for anæsthesia. When it is decided to give an anæsthetic, a finger should be inserted into the nasopharynx and placed in the choana of the nostril which is being examined, as it is possible to push the foreign body backwards into the nasopharynx, whence it may be either inhaled or swallowed. The finger in the nasopharynx will prevent such an accident and will also assist, in certain cases, in gripping the foreign body. If it is thought that the foreign body is radio-opaque, such manipulation should be preceded by an X-ray of the skull. Occasionally, if a foreign body has remained in the nostril for some time, it will form the core of a concretion. These concretions may be very large, and it may be found advisable to break them up before removing them.

### SINUSITIS

**Acute Sinusitis.**—In the treatment of sinusitis the aims are similar to those in affections of the nose, namely, the relief of pain and the restoration of function. The loss of ciliary function for a prolonged period may render treatment unavailing. If, therefore, surgical treatment is to be avoided, the early stages of the physiological derangement must not be neglected. As pain is so frequently the result of obstruction to drainage, the relief of pain in many cases becomes the problem of securing the release of contents obstructed within the sinus. As the sinus can only drain through the small ostium into the nasal cavity, treatment is primarily directed towards restoring the patency of the ostium. Agents are used which have the function of shrinking the mucous membrane of the nose. Of these, the simplest are steam inhalations containing menthol, which not only help to shrink the mucous membrane but also have an analgesic action and will relieve the accompanying discomfort. Ephedrine (1 to 2 per cent.) in isotonic saline solution may also be instilled into the nose. This will help to shrink the turbinates and will open up the œdematous middle meatus. These drops can be repeated at sufficiently frequent intervals to maintain a shrunken condition of the nasal mucous membrane, and may thus promote a flow of secretion from the sinuses. In certain cases where the turbinates show very marked engorgement, a pledget of wool soaked in cocaine (10 per cent.) can be inserted into the upper part of the nose against the middle turbinate. This causes a very marked retraction of the turbinate and will frequently be successful in relieving an obstruction.



It may have to be repeated, however, at frequent intervals, and it must be remembered that cocaine has a reaction which may defeat the original purpose of its application. Rest is of the utmost importance in the treatment of sinusitis, and a patient should always be advised to refrain from business or other activity, since return to health will be delayed if he insists on carrying on with his daily work. Another essential is that the patient should remain in the same temperature as far as possible, to prevent changes in the tension in the nasal mucous membrane. Accordingly, rest in bed is generally advisable, as this provides the easiest method of controlling the patient's activity; and should there be any constitutional disturbance, this must be insisted upon. For the pain itself, apart from analgesic drugs and measures which aim at the relief of tension within the sinuses, the application of heat in various forms is the most valuable way of relieving the patient. Radiant-heat baths will frequently cause an immediate diminution in the congested condition of the sinuses and relieve the patient. On the other hand, they may possibly increase the patient's discomfort; in such cases the radiant-heat baths should be immediately discontinued. Short-wave diathermy is also of value, though in the very acute stages this may cause even greater pain and is best reserved for the subacute stage when the sinusitis is commencing to clear up. Heat may be applied as fomentations over the affected sinuses, or, if available, electric pads may be used instead.

In the purulent stage of the infection, where there is considerable constitutional disturbance, the object of treatment should be to avoid operative interference if that be possible. Surgical measures should be reserved until the acute stage has passed. It may happen, however, that increasing severity of symptoms, such as swelling or increase of pain, may render it necessary to undertake some operative measure for the relief of the patient. Proof-puncture permits lavage or the introduction of penicillin through a fine catheter. Proof-puncture, however, in the stage of acute inflammation may be extremely painful, so that the question of anæsthesia, local or general, must receive careful consideration. This procedure has its greatest value where the sinus is filled with purulent fluid. In many cases of the most acute type, however, there is no cavity within the sinus, the whole space being occupied with œdematous mucous membrane. In which case proof-puncture will accomplish nothing except when it is used as a means of introducing a fine gum-elastic catheter into the sinus to facilitate the frequent instillation of penicillin. Penicillin may also be introduced by the displacement method of Proetz. Each case must be judged by the individual reaction to the procedure, but as a rule it should not be repeated within two or three days' time, and if after three or four punctures sufficient improvement is not obtained, it is obvious that proof-puncture is inadequate and further operative interference must be considered. It should be noted that the administration of prophylactic doses of sulphonamides (see p. 71) in infections of the upper air-passages has been found to reduce materially the incidence of sinusitis.

**Chronic Sinusitis.**—In chronic sinusitis it is frequently worth while to attempt to clear up the infection before having recourse to surgical means, for sometimes the symptoms are referable to a slight and intermittent degree of obstruction to drainage. Full investigation of these cases should be undertaken before treatment is finally decided upon. Where gross infection is shown by radiography, and where there is obviously polypus formation

within the sinus, then conservative measures are not likely to achieve cure and recourse must be had to surgery. Where, however, the infection is not severe, proof-puncture and lavage with saline solution may be sufficient to allow the cilia to recover function.

The displacement method of introducing agents within the sinuses is a useful one. It consists of applying suction to the nose in such a way that when the head is placed in a suitable position the ostia of the sinuses are submerged in the solution which is being introduced. The air is drawn out of the sinus by the suction, and the drug allowed thereby to find its way in. Ephedrine in saline ( $\frac{1}{2}$  per cent.) is frequently used in this way; by its gradual elimination it gives a prolonged action and keeps the ostium shrunk, thus allowing drainage over a considerable period. Short-wave diathermy, by causing a certain degree of hyperæmia within the sinus, may be effective in clearing up an infection which has not been too long established. The results of penicillin treatment in chronic sinusitis have been disappointing.

*Complications of Chronic Sinusitis.*—The chief complications of sinusitis which require treatment are osteomyelitis, abscess formation in the tissues outside the sinuses, such changes in the eyes as are induced by pressure either upon the orbit or upon the optic nerve, and meningitis. This last is a late complication due to extension of the disease. The treatment of these complications of sinusitis is mainly palliative, pending the arrival of surgical assistance (see also Penicillin, p. 86).

## THE PHARYNX

### TONSILLITIS

**Acute Tonsillitis.**—The treatment of this affection depends upon the stage to which the illness has progressed. In the earliest stages, where there is merely a hyperæmia of the tonsillar region, simple precautions may be sufficient to abort the disease. But it must be impressed upon the practitioner that this condition must never be treated as of small consequence, and fairly stringent regulation of the patient's activity at the beginning of the illness may save him from great trouble at a later date. As a working rule, one may say that if there is any general disturbance, such as rise of pulse-rate or temperature, a feeling of illness, malaise, or shivering, then the patient should be put to bed. Regulation of the bowels is a first consideration, but unnecessary purging should be avoided. Owing to his sore throat, the patient will, in all probability, limit his intake of fluid, and it is therefore unwise to increase fluid loss by excessive purging. Where there is rise of temperature, antifebrile drugs may be used, such as the salicylates. Treatment with sulphonamides or penicillin is fully discussed elsewhere (see pp. 71, 86). The local treatment consists chiefly of gargles and paints, which should be of a mild nature. There should be no nipping or burning with any of the drugs used. The mucous membrane is in an inflamed condition and requires soothing and not irritation. A gargle of carbolic acid, sodium sulphocarbonate, sodium bicarbonate and glycerin (see Appendix, p. 720) may be used.

Boroglycerin is a good paint for early acute cases. There may be, even in the earliest stages, a marked glandular involvement. The glands of the submaxillary and upper cervical region may be tender and swollen, limiting

thereby the movements of the neck. These conditions may be met by hot fomentations of boracic, poultices of linseed, or applications such as kaolin. These give relief and also reduce swelling.

In the follicular stage of tonsillitis, in which the tonsils are found to be spotted, treatment is frequently simpler, as at such a stage the patient is usually quite willing to retire to bed. The symptoms are rise of temperature and of pulse-rate, with associated pain and difficulty in swallowing. This may be so severe as to determine the nature of the patient's diet, confining it to ice-cream, junket and to fluids such as tea, barley water, glucose and orange juice, strained soup and porridge. Locally, gargles and paints are again required, and treatment of the glands of the neck should they be enlarged and tender.

In the membranous form of tonsillitis there is an extension of the infection from the above stage, and treatment has to be correspondingly energetic. The patient's general condition, as a rule, is weaker and his fluid intake is usually considerably limited owing to the extreme pain in swallowing. In such cases, if the patient does not seem to be taking sufficient liquid by the mouth, it must be given in other ways. This may take the form of a rectal saline, but the best method is the administration of glucose (5 per cent.) in normal saline by the continuous-drip system. In this stage of the infection, gargles are frequently ineffective, as the patient may lack the strength to use them. The membrane also frequently covers parts of the throat to which the gargle does not reach. Under these circumstances an antiseptic spray may be the best means of cleansing the infected parts. The spray may consist of hydrogen peroxide and water, in equal parts, or a solution of glycerin of thymol (see Appendix, p. 720). Another excellent method of treatment is the use of hot irrigations. Either hot saline or hot bicarbonate of soda solution can be used for the irrigation. A Higginson's syringe is boiled and a pint of saline at least will be required. The patient's head is placed in a dependent position over a basin placed at the side of the bed and with the Higginson's syringe the throat is douched with the hot fluid. This efficiently cleanses the mucous membrane and is a great comfort to the patient. Soothing paints, also, are excellent, because they help to ease the local condition and stimulate swallowing and the flow of saliva. Inhalations may be required because the inflammation is seldom localized and there is frequently hyperæmia of the larynx. A useful inhalation consists of 15 to 20 drops of compound tincture of benzoin (Friar's balsam) in 1 pint of hot water.

It is important to maintain as much movement as possible in the throat and to keep the surfaces constantly cleansed. It is for this reason that sprays are of such value, for, even if the saliva is deficient, they induce swallowing movements or the coughing up of infected material. In children, especially, the spray is useful when the throat becomes really sore. A child sometimes refuses to gargle or drink, and it is in these cases that the greatest danger occurs from dehydration. Further, the throat is held completely quiet so that the infection becomes severe and there is little or no cleansing of the parts locally. In order to spray the throat, a certain amount of restraint may be required to control the child properly, and, as it is unlikely that the mother will be able to carry out this treatment adequately, it is usually best to have these cases under the charge of a nurse or to place them in hospital. An excess of affection has before now been responsible for tragedy in the case of a child.

*Complications.*—Of the complications of tonsillitis, peritonsillar abscess or quinsy is the most frequent. In the early stages, in which the tonsillar region is slightly swollen and the soft palate is showing only a little sign of oedema, palliatives are indicated, such as frequent hot gargles and fomentations to the glands. Sleep is usually interfered with, and it is an excellent thing to give a sedative at night in order to conserve the patient's strength. The systemic administration of penicillin (see p. 86) at this stage frequently causes regression of the inflammation without the formation of pus. The question frequently arises as to when is the correct time for surgical assistance. It may be said that when the soft palate has a distinct bulge on one side and the tonsil is pushed towards the mid-line, then an attempt may be made to locate pus behind the tonsil. Many cases are seen only when there is an obvious bulge in some part or other of the swollen soft palate. In such cases it is a simple matter to push a pair of blunt forceps into the soft swelling and evacuate the pus. Where, however, no point of softening exists, the peritonsillar abscess is best opened from the superior tonsillar crypt. A long pair of blunt-pointed forceps is used. If desired, the throat may be sprayed with cocaine (10 per cent.), or an anæsthetic lozenge may be given to the patient to suck. This rarely has the effect of lessening the pain of the opening of the abscess, but it frequently diminishes the amount of trismus present and helps to give the patient confidence. The forceps are inserted into the superior tonsillar crypt and pushed sharply upwards and outwards through the capsule into the abscess cavity, and widely opened. This is followed by a gush of pus and the patient experiences a very great sense of relief. Hot gargles are given and treatment continued as before until the swelling has disappeared from the side of the throat.

Abscesses may occur in other parts of the throat as the result of tonsillar infection. These are more frequent in young children. They occur either in the nasopharynx or in the hypopharynx, and their treatment demands evacuation at an early stage of the infection. Correct treatment is of the utmost importance, and the possibility of this affection being present should never be lost sight of in unexplained illnesses in young children, where there is difficulty in breathing or swallowing. In all cases of acute tonsillitis and its complications, when general infection is marked, the use of sulphonamide is of the greatest value in reducing the toxæmia accompanying the infection.

*Chronic Tonsillitis.*—Chronic tonsillar infection occurs with comparative frequency in adults, but many are unaware of their disability. These patients are symptom-free, because they have acquired immunity to their infection, and it is not until some general infection, or lowering of resistance, causes a breakdown of the immunity, that symptoms appear which demand attention. The use of palliative treatment in such a case is to enable the immunity to be built up again.

Palliative treatment may consist of painting the tonsils; in cases of chronic tonsillitis such paints are of a faintly irritating character, the commonest of these being Mandl's paint. Gargles may be recommended, as they serve the purpose of exercising the pharyngeal muscles and ensuring an adequate blood supply to the parts concerned. In such cases, also, suction is recommended as likely to remove the debris and infected material from the tonsil and, no doubt, as far as the surface is concerned, it will do so. But a consideration of the anatomy of the tonsil will suggest very strongly that the tortuous channels of small size which constitute the crypts

are not likely to be adequately evacuated by any method of surface suction. Radiation of various kinds has been used in tonsillitis; ultra-violet and infra-red may be applied directly to the tonsil by means of the Kromayer or other lamp with special applicators. These produce hyperæmia within the tonsil, and the increased blood supply may reasonably be expected to deal with some of the earlier forms of infection. Where, however, infection has been established over a prolonged period, with the usual fibrous tissue formation and replacement of columnar epithelium with other forms, such treatment is unlikely to reverse the established pathological changes. Gamma radiation has been recommended for treatment in inflamed tonsils, and there is no doubt that radiation will remove tonsillar tissue, if used in sufficiently large doses. But it is equally evident that if used in sufficient dosage to destroy the tonsil, the side-effects are such that the treatment does not justify the expenditure of the time and money required. Either the reactions are severe—very much more so than with a simple tonsillectomy—or the treatment is so prolonged that the expense will be a very serious consideration.

The technique of removal of the tonsils does not fall within the scope of this section, but the practitioner may have to make the decision as to when the tonsils should be removed, and to know the appropriate method. Operations for tonsillectomy are many and the details vary according to the ideas of the surgeon concerned, but they all aim at the complete removal of the tonsil and its surrounding capsule. The tonsil may be dissected out from its bed or may be removed completely by diathermy coagulation. The coagulation technique has received prominence of recent years and considerable claims have been made for it. The complete removal of the tonsil by coagulation involves some half a dozen sittings and occupies a considerable period of time.

There is practical unanimity of opinion that removal by surgical dissection is the quickest and most satisfactory method. The disadvantages of the operation are that the patient is confined to bed for some days and has to cease work during that time. He is subject to a certain amount of operative risk, possibly to an anæsthetic and to the psychological upset inseparable from the idea of an operation. The advantage of the coagulation method is that the patient need not necessarily be off work, that the treatment can be carried out in the consulting room or office, and, though frequently painful, is not so incapacitating as operation and can be applied in cases where the physical state of the patient contraindicates surgical measures. The outstanding disadvantage of the method is that it is impossible to guarantee complete removal of the tonsil in every case. Diathermy coagulation has no selective action upon the tonsillar tissue, and if complete coagulation of the tonsil is guaranteed, it is impossible to ensure that the deeper structures of the throat are left unharmed. The treatment tends to be lengthy and is frequently more painful than those carrying it out are wont to admit.

### PHARYNGITIS

The treatment of pharyngitis is a twofold problem. In the vast majority of cases of pharyngitis, we are concerned with a remote cause which is having a local effect. It is essential in the first instance to inquire with care into the patient's habits, surroundings and type of work. Habits, particularly

with regard to smoking and alcohol, require investigation. The presence or absence of gastric trouble, rheumatism and like diseases may modify the attitude towards treatment. Excessive dust or a special type of atmosphere may be found to be of ætiological importance. For instance, the presence of ammonia fumes or other forms of irritant may require to be eliminated before treatment can be successful. Inflammation or suppuration in other parts of the upper air-passages may be causing the pharyngitis. One of the commonest of these causes is a sinusitis, and the sinusitis will require treatment before any improvement can be expected in the pharynx. Treatment of chronic tonsillitis may be necessary, though it should be noted in this connection that the removal of tonsils for the cure of pharyngitis should not be undertaken, except after most careful consideration, as in most cases the tonsillectomy will tend to aggravate the chronic pharyngitis rather than to improve it.

The local treatment of pharyngitis depends upon whether the condition is acute or chronic. Gargles are rarely of value in an *acute pharyngitis*, apart from helping the flow of saliva and assisting in the lubrication of the mucous membrane. Sprays and paints of boroglycerin or glycerin and tannin are of real value. Steam inhalations are soothing in the more severe types of case. These may be medicated, as, for instance, with Friar's balsam. Lozenges containing menthol or other drugs are soothing to the patient. Where inflammation is severe, irrigations should be employed (see p. 706). Inflamed and tender glands require treatment by fomentations or other form of heat. Sulphonamide or penicillin therapy should be instituted immediately. In the *chronic stage*, treatment is more of the nature of counter-irritation, and such application may be made to the pharynx locally as will help to stimulate the resolution of the inflamed mucous membrane. Paints, such as Mandl's paint, or the careful touching of the inflamed portions of membrane with iodine or with silver nitrate (10 per cent.), will help to reduce the irritation. The cautery or diathermy, also, may be used to destroy the red lymphoid nodes in the pharyngeal wall. These measures, however, must be employed with the greatest care. If the cautery is employed the throat should be painted with 10 per cent. cocaine, after which the fine cautery point may be used very sparingly on the enlarged lymph nodes.

**Retro-pharyngeal Abscess.**—The difficulties caused by retro-pharyngeal abscess are chiefly those of diagnosis; but where obstruction of the naso-pharynx or larynx is being caused by abscess formation, the relief of the obstruction is the treatment immediately required. The abscess, if causing obstruction, must be opened, and this may be done by the oral route, except in the case of abscesses which have their origin in tuberculous cervical caries.

### NEUROSES OF PHARYNX

**Sensory Neurosis.**—Paræsthesia, or the underlying cause of paræsthesia, may be found to be some degree of pharyngitis or enlargement of lingual tonsil and, in such cases, removal of these is the first step in treatment. The majority of patients who appear for treatment for this unpleasant sensation in the pharynx are cancer-phobes, and in such cases one of the most important parts of the treatment is the suggestion to the patient that there is no underlying disease and that a little local treatment is probably all that is required.

**Anæsthesia of the Pharynx.**—This condition usually accompanies lesions of the base of the brain, and therefore is not amenable to treatment.

**Glosso-pharyngeal Tic.**—The treatment of glosso-pharyngeal tic falls into the category of surgical treatment and consists of nerve section.

#### PATERSON-KELLY SYNDROME (PLUMMER-VINSON)

The symptoms of dysphagia will usually clear up rapidly under appropriate treatment for the associated anæmia (see p. 466 *et seq.*). Only when these measures are unsuccessful does local treatment of the obstruction become necessary. This consists in stretching the stricture through a laryngoscope or œsophagoscope. The blind intubation of these patients is to be deprecated, and, in the first instance, treatment should be carried out under direct vision by those experienced in such procedures.

## THE EAR

### DISEASES OF THE EXTERNAL EAR

**The Auricle.**—*Injuries.*—Hæmatoma of the auricle calls for treatment on account of its unsightliness and the possibility of subsequent infection with destruction of the cartilage. Where large, it is best treated by aspiration of the swelling, with proper aseptic precautions. The ear should be cleaned with spirit and a hypodermic syringe and needle should be inserted into the auricle and blood-stained fluid withdrawn. This should be repeated if necessary. The ear should then be bandaged firmly, or, if inflamed, should be covered with an ichthyol and glycerin soak (10 per cent.).

*Perichondritis.*—When inflammation has supervened, treatment consists in the application of soothing remedies. Ichthyol and glycerin (10 per cent.) or boric fomentations should be applied; and if pus forms, it should be evacuated.

**Skin Affections.**—*Furunculosis*, or hair-follicle infection, calls for soothing treatment in the first stages. The ear should be packed with gauze soaked with ichthyol and glycerin and heat applied outside the ear in the form of boric fomentations or a thermal pad. Short-wave diathermy may be used in an effort to abort the abscess or to cause it to develop quickly. It is better to avoid incision as far as possible, but where the furuncle is very large and pus has obviously formed, then incision may be undertaken.

*Otitis Externa.*—The treatment of otitis externa varies according to the stage of the disease and its particular type. In many of these cases the ear is filled with discharge and debris: it may therefore be essential to cleanse it by syringing. If possible this course should be avoided, and if syringing has to be resorted to, the ear should be carefully dried afterwards.

In the very acutely inflamed type, where there is some perichondritis, the treatment should be the same as that outlined for furunculosis. When the most acute stage has passed, then the ear should be packed with strips of gauze soaked in aluminium acetate solution (8 per cent.). The same solution is used for the drier and more scaly types of infection; it soothes and quickly dries up the skin. To cause the condition to clear up finally, a useful application is 2½ per cent. alcoholic solution of gentian violet. The external meatus should be swabbed with this solution, and the solution should be dried in the meatus by a blower.

**Wax in the Ear.**—Wax in the ear is removed by syringing. Where the wax is very hard, before syringing it should first be softened by the instillation of drops of saturated solution of bicarbonate of soda. Half a dozen drops of this should be instilled four or five times for one to two days preceding the syringing. The syringing of the ear may be carried out either with an ear-syringe, which should have finger-rings, or, in default of this, with a Higginson's syringe. The temperature of the syringing fluid is of importance and the optimum temperature is blood heat, for by the use of such a temperature, unpleasant effects upon the internal ear are avoided. Warm water, preferably boiled, is quite effective, or tap water with a few drops of antiseptic added may be used. The patient should be instructed to hold the basin or kidney-dish underneath the ear to catch the waste water, and a trough which fits around the ear will be found of great advantage in avoiding splashing. Unless the person carrying out the treatment is experienced, a syringe with a sharp nozzle should not be used as this is liable to damage the meatal wall. The stream of water should be directed against the posterior superior aspect of the meatal wall. By doing so the plug of wax is loosened and the water passing behind the wax tends to force the plug outwards. Great force must not be used, and if considerable difficulty is being experienced, it will assist if the posterior edge of the wax plug be elevated from the meatal wall to make a point of entry for the stream of water. During the syringing frequent inspection of the meatus should be made in order to ascertain the progress of the removal.

After the plug of wax has been removed the ear should be dried of excess fluid. If, as sometimes happens, some epithelium is removed along with the wax and a raw place is left on the meatal wall, it is wise to pack the ear with a strip of gauze soaked in aluminium acetate solution (8 per cent.) for twelve hours to prevent the possibility of infection. Where there is known to be a perforation in the drum, wax should not be removed by syringing, but preferably by being picked out if necessary after softening. Where there is a perforation of the drum there is a possibility of the water passing through into the middle-ear cleft and setting up an acute inflammation.

**Keratosis Obturans.**—This condition consists of the impaction of a very large plug of wax in the inner part of the external meatus with subsequent epithelial destruction by pressure. The hardness of the plug may be such that a general anæsthetic may be required to accomplish its removal.

**Foreign Bodies in the Ear.**—From the point of view of treatment, foreign bodies in the ear may be divided into three classes—vegetable, mineral and animal.

Vegetable foreign bodies, *e.g.*, a pea, should not be removed by syringing. If the initial syringing is unsuccessful, the foreign body will swell with the water and give the patient excruciating pain, and also render the subsequent removal extremely difficult. Mineral foreign bodies, such as glass beads, are most easily removed by syringing. If this fails, a proper equipment of ear-forceps, hooks, etc., is required for their safe removal. Insects and such animal foreign bodies should be killed first by the introduction of spirit drops or chloroform vapour, and then syringed out. In small children, anæsthesia is frequently required for the safe removal of the foreign body. It is useless to attempt to remove a foreign body from the ear of a kicking, struggling child. In such cases the proper preparation should be made for



the anæsthetic. A lengthy administration may be necessary, since some foreign bodies may tax the ingenuity and the patience of the operator if they are to be removed without damage to the drum.

### AFFECTIONS OF THE DRUM

**Rupture of the Drum.**—Whether this occurs as a result of a concussion, for example from a blow or gun-fire, or from a fracture of the skull, the main principle of treatment is inactivity. A piece of sterile wool should be inserted in the meatus and no syringing or cleansing of any kind permitted. The prophylactic use of penicillin or the sulphonamides will help to prevent suppurative complications. In cases where rupture has taken place and suppuration, as may frequently happen, sets in, then the treatment is the same as that of conservative treatment for acute otitis media, to which the reader is referred.

**Myringitis Bullosa.**—Very large hæmorrhagic blisters may occasionally be opened, but as long as the hearing is good and the constitutional disturbance is slight, soothing drops—for instance, anhydrous glycerin to which carbolic acid (4 per cent.) may be added—should be instilled.

**Herpes.**—Herpes of the auricle and meatus may occur as part of herpes zoster oticus (Hunt's disease). The local condition is treated as in otitis externa, the chief symptom requiring attention being pain.

### DISEASES OF THE MIDDLE EAR

**Acute Otitis Media.**—In acute otitis media treatment is required on account of pain, deafness, discharge from the ear and constitutional disturbance. The condition, from the point of view of treatment, falls naturally into two sections: firstly, treatment of acute otitis media before discharge appears in the ear; and, secondly, after discharge has made its appearance.

*Acute Otitis Media before Discharge.*—Pain is the chief complaint. As this pain is due to irritation of nerve-endings in the acutely inflamed and tightly stretched drum membrane, direct application to the inflamed membrane may be made by means of anæsthetic drops. One of the most useful forms of application is anhydrous glycerin containing 4 per cent. carbolic acid. Heat is a favoured form of application, and warm drops of oil have been used traditionally as a soothing application to the ear. This, however, is not a good method of treatment, as the ear is liable to be damaged by such instillations. Heat applied, as a fomentation of boric lint wrung out of hot water or a saturated solution of magnesium sulphate, outside the ear, is equally effective.

Constitutional symptoms also call for treatment. The rise of temperature and pulse-rate with a general feeling of illness should be met by confining the patient to bed. In cases of constipation, treatment should begin with a purge, though violent purging should be avoided. Fluids should be given freely; starvation is not indicated, and the patient should be given a good sustaining diet. Drug treatment should not include antifebrile drugs. The administration of such drugs as aspirin, antipyrin, etc., may bring the temperature down, but at the same time they so obscure the clinical picture

that it is difficult to form an accurate estimate of the progress of the infection. If the pain is severe, it may be relieved by analgesics. Sulphonamides or penicillin should be given from the beginning of the illness. (For full instructions see pp. 71, 86.)

*Treatment after the Discharge Appears.*—The chief principle in treatment at this stage is the encouragement of the free flow of discharge. In addition to promoting the flow through either the perforation or the paracentesis opening, an endeavour must be made to promote the reopening of the natural drainage channel—the Eustachian tube. Once discharge is established, nature must be assisted in drying up the secretions.

There are two principal methods of treatment of this type of affection, and there are two distinct schools of thought regarding the proper method of management. These methods are referred to as the dry method and the wet method. The dry method aims at introducing nothing into the area which is likely to convey sepsis into the middle ear. The wet method consists in cleansing the ear with the simplest form of apparatus, namely, the syringe, and then adopting measures as in the dry method which will help nature to dry up the discharge. The dry method entails a considerable amount of attention. The ear has to be cleansed carefully under direct vision at frequent intervals. In one of the most successful methods a wick of wool or gauze is inserted into the meatus, close to the perforation, so that it acts by capillary attraction in withdrawing fluid rapidly from the middle ear. The ear may then be mopped dry at intervals, and drying drops instilled, *e.g.*, rectified spirits containing a little boric acid.

In the dry method, nothing is gained by mere wiping of the outer part of the ear. The ear must be dried right to the drum and all excess of secretions and debris must be removed so that a completely clear channel is left for the discharge. In addition, the external meatus must be wiped with antiseptic before mopping the ear, so that sepsis is not transferred from the outer part to the inside of the ear.

The wet method of treatment consists of instilling into the ear drops of peroxide of hydrogen which by their action tend to loosen the discharge which accumulates in the ear. This discharge is then syringed out with an antiseptic lotion. This may consist of boric lotion, lysol (1 teaspoonful to a pint of water) or other weak antiseptic. After syringing, the ear is mopped dry as far as possible and, if desired, drying drops are instilled into the ear.

The relative value of these methods is worth consideration on account of statements having been made that it is almost a malpractice to syringe the ear when it is the seat of an acute otitis media. Theoretically, the dry method is the best for dealing with an ear suppuration, but it presupposes a knowledge and a skill which is not to be expected or demanded from the average nurse. In cases in which treatment is carried out at home or has to be done by an overworked district nurse, the wet method has a distinct advantage and is widely used in certain clinics, notably in Scotland, where the distressing results assumed by some writers have never been observed.

Besides the methods detailed above for improving the condition of the ear, other means may be used for withdrawing discharge from the middle ear. When available, suction is of use in skilled hands. The ear may be cleared to some extent of discharge by catheterizing the Eustachian tube

and blowing air through the middle ear. This should not be done in the earlier stages of the disease, but is useful for helping to empty the middle ear when the disease is beginning to resolve. Inflation of the Eustachian tube must always be done at the end of treatment. After the ear is dry, the hearing in the majority of cases is subnormal and inflation of the Eustachian tube will do a considerable amount towards restoring it to normal and, in many cases, will prevent permanent deafness. This inflation should always form the last step in the treatment, and must never be neglected.

*Indications for Paracentesis.*—Although paracentesis is a surgical procedure, it must sometimes be undertaken by those who are at a considerable distance from hospital service, and it is therefore essential that the medical practitioner undertaking the treatment of acute otitis media should have a clear idea of the conditions which demand this procedure. One of the first effects of an acute infection on an ear-drum is the production of pain, owing to the irritation of the nerve-endings by the inflammation and the tension; if the pain becomes excessive, relief may be obtained by paracentesis. Secondly, if there is increasing toxæmia with obvious middle-ear infection and the tympanic membrane is bulging, relief may be expected by the release of the contents of the middle ear. Again, if a drum is evidently upon the point of perforation, indicated by a yellowish area appearing at the most prominent part, immediate relief by paracentesis may obviate the sloughing of the drum membrane; a surgical cut so made will heal rapidly, causing less permanent damage to the drum structure than if a portion of the membrane is allowed to slough out. Where deafness is becoming more marked, owing to increasing tension in the middle ear, paracentesis may afford the most certain method of ensuring rapid and complete return of hearing.

In the treatment of these cases of acute middle-ear infection, one principle must always be observed, *viz.*, that treatment is to be directed towards the prevention of deafness: we can do little or nothing for a patient once the hearing has been lost for a period. In this case above all others, prevention is better than cure.

An adequate source of light is required to carry out paracentesis. This may be obtained either from an electric lamp, the light from which may be focused upon the ear by means of a head-mirror, or it may be obtained from an electric auriscope. Before carrying out a paracentesis the ear must be cleansed thoroughly and completely so that a clear view of the drum-membrane is obtained. General anæsthesia is advisable in all cases. When the patient has been properly anæsthetized, a paracentesis knife is introduced and the drum is incised in the posterior half in the form of a J, the upright portion commencing a little below the posterior horizontal fold of the drum and the incision being brought round in the lower part to finish just below the handle of the malleus. This procedure must, of course, be carried out with proper aseptic precautions, and the after-treatment is that for discharging ear.

*Complications of Acute Otitis Media.*—Treatment of complications of acute otitis media is essentially surgical, though chemotherapy is an important and indispensable adjunct.

**Chronic Otitis Media.**—Treatment of this condition depends to a great extent upon the type of suppuration, the part of the ear cavity which is

affected, the duration of the condition and the presence or absence of bone disease. It is obvious, therefore, that an adequate knowledge of the state of affairs in the middle ear is essential for the proper planning of the treatment. In the consideration of such a case the circumstances of the individual must not be overlooked, and treatment should be selected with regard to these circumstances, as, for instance, the patient's means and the conditions of his work, as well as from considerations demanded by the nature of the suppuration.

The treatment of chronic otitis media has three chief aims, of which the first and most important is the assurance of safety to the patient. The preservation of hearing is next in importance, for hearing is usually the equivalent of earning-power. Lastly, provided the first two conditions are satisfied, treatment should reduce to a minimum the loss of working time. Both surgical and conservative treatment play a part in the cure of chronic otitis media. Surgical treatment is essential in the presence of certain complications, such as brain-abscess, labyrinthitis, necrosis of bone and extensive cholesteatoma formation. The selection of the type of operation will fall upon the surgeon, who will make his decision in view of the conditions present and in keeping with the principles which have just been laid down.

*Conservative Treatment.*—This must be regarded as the method of choice. If a polypus is present in the ear, this may be removed, and granulations may be scraped or touched with silver nitrate or chromic acid. The object in view in the treatment of chronic otitis media is to dry up the discharge. To do this, the ear must first be cleansed of accumulated debris, wax, etc.; secondly, drying agents are instilled into the ear; and, thirdly, special forms of treatment may be used. To cleanse the ear, peroxide of hydrogen drops can be instilled in order to loosen any accumulated debris. This should then be syringed out with boric lotion or other mild antiseptic. In cases of very copious discharge, this may be done morning and evening, but in most cases, once daily will be found sufficient. Syringing is sometimes carried out in special ways: where the chief infection is located in the attic, a cannula may be introduced into the attic region which is then syringed out. In the same way, syringing may be carried out through perforations. Drops, instilled into the ear, have for their objects antiseptics and the drying up of the discharge. The simplest method is the introduction of spirit. This may be rectified spirit or industrial spirit. It is usually combined with a small quantity of boric acid. About 5 to 6 drops are allowed to run into the ear from a warm teaspoon or dropped in from a fountain-pen filler. This should be done once or twice daily, according to the amount of discharge, and where syringing is being carried out, should form the last stage of the treatment. In certain cases attempts have been made to introduce agents via the Eustachian tube, such as mild silver protein (B.P.C.), silver protein (B.P.) and oils of various kinds. In addition, powders are used, with the object of drying up the ear. The simplest powder for this purpose is boracic acid powder. This is blown into the ear from a powder-blower. The use of boric acid powder with 0.75 per cent. of iodine is an improvement upon plain boracic acid. The principle of this treatment is that the boracic acid dissolves in the discharge of the ear and liberates nascent iodine, which exercises a powerful antiseptic action and assists materially in drying up the discharge. These powders should not be used in the early stages of

treatment because, if there is a great deal of discharge, they will merely block the ear; they are most useful during the later stages of treatment, when the ear is almost dry. A large quantity of powder should not be used, but only sufficient to produce a satisfactory coating. The use of penicillin in chronic otitis media has proved very disappointing.

Special forms of treatment are sometimes used, as, for instance, ionization. In some hands this treatment gives beneficial results. It consists in passing an electric current through the ear, using zinc as the positive pole in the ear. The application of the zinc is carried out by filling the ear with zinc sulphate solution, 2 to 4 per cent., and placing in the zinc sulphate solution the positive zinc pole. Before carrying out this treatment the ear must be cleansed with the utmost care, and dried. Where there is a perforation, special precautions must be taken to make sure that the middle ear is completely filled with zinc sulphate solution. This is done either by massaging the solution into the ear, to exclude air bubbles, or in certain cases where a perforation exists, a cannula is used to introduce the solution into the middle ear. Current to the extent of 5 ma. is used for ten to twenty minutes. Three or more applications may be required to obtain a good result. This treatment is particularly useful in young people, such as school children, but is quite useless where extensive disease exists, in particular bone disease or granulation formation.

**Progressive Middle-ear Deafness.—*Otosclerosis and Chronic Adhesive Process.***

—On general principles any obvious septic condition in the nasopharynx or pharynx should be eliminated. Any pathological state in the nose predisposing to catarrh or the incidence of colds should also be corrected. This is particularly advisable as otosclerosis and chronic adhesive process may be indistinguishable in the early stages, and the latter is believed to have its origin in ascending infections of the Eustachian tube.

Treatment of this condition has been given a new impetus by the development of the fenestration operation. This procedure can restore hearing to a practical level in a large proportion of those suffering from middle-ear deafness. The operation aims at restoring mobility to the labyrinthine fluids by replacing the closed oval window by another mobile opening in the ampullary part of the horizontal canal. This is accomplished by an operation which resembles a modified radical mastoid technique.

The most suitable patients for this treatment are young people under thirty years of age with normal tympanic membranes and deafness of pure middle-ear type. The contraindications to it are the presence of nerve deafness, past or present suppuration in the middle ear and extreme degrees of deafness. As only a limited amount of hearing can be restored by the operation, the improvement so obtained in very deaf people is insufficient to restore their hearing to a practical level. In suitable cases in young persons successful results may be achieved in eighty per cent. of cases treated, but as age advances the presence of senile nerve deafness progressively limits the advantages which can be obtained. Patients over fifty years of age are usually unsuitable subjects for the operation.

In the past it was found that the results of the operation were temporary—a great many cases relapsing after about two years—but with improvements in surgical technique results are permanent in the majority of cases treated. Where failure is due to osteogenic closure of the new opening, surgical revision of this can restore hearing to its former level.

## DEAF AIDS

When we are unable to prescribe treatment which will cure patients of the foregoing forms of deafness, we can do something to assist them to hear, since the practitioner is often asked for advice regarding artificial aids to hearing. A knowledge of such instruments is therefore essential to every practitioner.

There are two chief classes of aid—the mechanical and the electrical. The first group includes the familiar ear-trumpet, auricles and artificial drums. The second includes electrical and valve instruments. The advantage of the mechanical instrument lies in its lightness and portability and the fact that there is no upkeep. Its disadvantage is, however, that it is comparatively limited in its scope, and while such things as auricles may be concealed in the ear, the old-fashioned trumpet, although for many cases the most satisfactory form of hearing-aid, is so conspicuous that many patients refuse to use it. The auricle is, in effect, a miniature trumpet or shell which collects the sound and transfers it to the ear. Artificial drums may consist of small pledgets of wool soaked in glycerin or paraffin, etc., or they may be small discs of oil-silk which are introduced into an ear in which there is a perforation of the drum, in order to close up the deficiency in the drum-membrane. In certain instances they do excellent service.

Of the electrical aids, from the point of view of performance, the valve instrument is very much superior to the old non-valve telephone type. The valve instrument may consist of one or more valves, and as scientific instruments these have reached a high pitch of perfection. They give powerful amplification, and the electric circuits can be so adjusted that a particular part of the hearing range can be amplified to correspond with the greatest deficiency in the patient's hearing. The disadvantages of these aids are their expense and their bulk. Modern development, however, is helping to produce aids which are very much smaller than formerly; some can be divided into portions which may be carried in the pockets about the person. They require a considerable amount of battery renewal, but the batteries are becoming readily procurable in any part of the country. The type of patient likely to benefit from a hearing-aid is the young person who finds it essential to work for a living and whose deafness is beginning to make this difficult. It is these people who are likely to take the small amount of trouble which is necessary to understand these instruments and to get the best out of them. Those suffering from middle-ear deafness are particularly favourable cases for the use of electric hearing-aids. Elderly people suffering from nerve deafness are not generally successful in using these instruments. They are sensitive in regard to their appearance, and as a rule do not take the trouble to understand them well enough to obtain good results. The majority of these people are past the necessity for earning their living and regard their hearing more in the light of a social amenity than as a means of livelihood.

It is recommended that these instruments should be obtained on approval for adequate trial at home before they are finally purchased. This will entail a small fee which will be deducted from the purchase price if the instrument is retained. All the firms on the register of The National Institute for the Deaf will make this concession. The price of these instruments

will vary from a matter of shillings in some of the non-electrical types to over £20 for the more elaborate instruments.

## THE LARYNX

### LARYNGITIS

**Acute Laryngitis.**—This condition is usually part of a general infection of the upper air-passages, and treatment of laryngitis in a great many cases must include the treatment of the upper respiratory infection also. The first principle of treatment of laryngitis is rest of the larynx. This is essential for the rapid cure of the condition and to prevent the acute stage from lapsing into that of a chronic laryngitis. One of the commonest causes of acute laryngitis is the use of the voice in the presence of an inflammation of the upper air-passages. Resting the larynx involves not only the avoidance of vocal function but also the avoidance of muscular effort. As a considerable muscular effort is required from the larynx every time the thorax is braced or the arms used vigorously, movement will frequently cause effort in the larynx and this must be prevented. For this reason the patient is best nursed in bed, even although constitutional symptoms may not seem sufficiently severe to demand this treatment. This has the further advantage that the patient is kept in an even temperature, which is another important point in treatment.

General febrile conditions will be met by antifebrile measures, laxatives, etc., as for coryza. Locally the inflamed larynx must be soothed. This may be done by steam inhalations, sprays and direct applications. Steam inhalations may be medicated, and if so, with soothing and not with irritating agents. Tinct. benz. co. is one of the most useful of these: 15 to 20 drops should be placed in half a jug of very hot water and the steam inhaled for fifteen minutes at a time.

Sprays may be of light oils and may contain essential oils to make them pleasanter to the larynx and trachea. Oily solutions may be applied directly to the larynx by means of a dressed probe.

Frequently there is acute pain in the neck, and applications of heat—kaolin poultices, linseed poultices, thermal pads, etc.—give comfort and relief.

**Chronic Laryngitis.**—The first step in the treatment of a chronic laryngitis consists in systematic search for the exciting agent. The removal of the cause of the irritation is essential. If it is impossible to identify any one cause, then all sources of irritation must be eliminated, such as tobacco, alcohol, the presence of fumes, frequent contact with dust, etc. The voice should be put at rest for a period, provided the patient's economic condition will permit. Inhalations of tinct. benz. co. should be prescribed to be used at night-time only, and a soothing spray can be used frequently throughout the day.

Locally the larynx can be painted with mild preparations, and in very chronic and resistant cases a weak solution of silver nitrate ( $2\frac{1}{2}$  per cent.) or zinc sulphate (5 to 10 per cent.) may be tried. This, however, must be used with the utmost care. Complete examination of the upper respiratory passages must always form part of the preliminaries to treatment, as a sinusitis or other infection may be found which will require treatment before any improvement can be expected in the laryngeal condition.

If it is possible to change the patient's environment, this is frequently a valuable measure, and in such circumstances warm, south-westerly exposures should be chosen.

### ŒDEMA OF THE LARYNX

The proper management of patients suffering from œdema of the larynx may on occasion render surgical intervention unnecessary.

The commonest type of case demanding treatment is that which follows inflammation. This may be due to a variety of causes such as diphtheria, primary septic infection of the larynx, abscess or infection of the respiratory tract above the larynx, chronic disease around the larynx, or reactions to trauma of various kinds. In such cases steam inhalations are soothing; sprays of mild antiseptics such as glycerin of thymol or hot irrigations of bicarbonate of soda solution are also helpful, particularly when the inflammation has commenced in the pharynx. Hot fomentations or ice packs applied to the neck may be of service. It must also be remembered that severe dysphagia may limit the patient's fluid intake and thereby increase toxæmia. In such circumstances intravenous infusion of saline may be necessary, and should not be employed only as a last resort. Where there is the slightest suspicion of diphtheritic infection, antitoxin must of course be given at once (see p. 20).

Where œdema of the larynx is due to non-inflammatory causes, such as urticaria, drug reactions and certain systemic diseases such as nephrosis, attention must of course be directed to the primary disorder. In acute urticarial œdema subcutaneous injections of 5 to 8 minims (0.3 to 0.46 c.c.) of adrenaline usually bring rapid relief. Locally a spray of 1 in 1,000 adrenaline solution, with or without the addition of 10 per cent. cocaine solution, is helpful. If the necessary instruments are available, scarification or puncture of the ballooned tissue may be undertaken in severe cases. In less urgent cases the use of antihistamine drugs (see p. 96) is the treatment of choice.

When conservative measures have failed it becomes necessary to resort to intubation or tracheotomy. The point at which such treatment is demanded depends partly on the rapidity of progress of the œdema and partly on the response of the patient's circulation to the increased strain upon it. A rising pulse-rate is always a danger sign and, if in an afebrile adult the pulse exceeds 100, preparation should be made for intubation or tracheotomy. The method chosen will depend on the cause of the œdema: if rapid recovery can be anticipated, as in urticarial œdema, then intubation with a soft rubber tube is the method of choice; but if, owing to inflammation or some other cause, immediate recovery cannot be expected, then tracheotomy is necessary. It should be emphasized that tracheotomy should not be delayed until it is a final desperate measure to save life, but should be undertaken as a deliberate surgical procedure. In many cases of inflammatory origin the relief of obstruction to the airway is not the only benefit which accrues from tracheotomy, since it gives an opportunity for efficient drainage of the lungs by suction, and in a toxic enfeebled patient the conservation of energy, secured through the replacement of coughing by suction, may be decisive in the patient's favour.



## APPENDIX

## NOSE

- R Sod. Bibor.  
 Sod. Bicarb.  
 Sod. Chlorid. . . . . āā dr. 2 (7·8 gm.)  
 Sig.—One teaspoonful to a pint of warm water.

- R Menthol . . . . . 0·5 per cent.  
 Ol. Limon. . . . . 0·5 per cent.  
 Paraff. Liq. . . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—Use in an atomizer.

- R Ephed. Hydrochlor. . . . . 1 to 2 per cent.  
 Glucos. . . . . 4 per cent.  
 Normal Saline . . . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—Use in an atomizer.

## EAR

- R Solution of aluminium acetate . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—Soak  $\frac{1}{2}$  in. ribbon gauze in solution and pack  
 into the ear once daily.

- R Ichthammol in glycerin, 10 per cent. . fl. oz. 1 (28·4 c.c.)  
 Sig.—Soak  $\frac{1}{2}$  in. ribbon gauze in solution and pack  
 into the ear once daily.

- R Iodi resublimati . . . . . 0·75 per cent.  
 Pulv. Acid. Boric. . . . . oz. 1 (31 gm.)  
 Sig.—Use in a powder-blower as directed.

- R Acid. Boric. . . . . gr. 15 (0·9 gm.)  
 Sp. Rectificati . . . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—Ear drops.

- R Scarlet red . . . . . gr. 25 (1·5 gm.)  
 Sp. Rectificati . . . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—10 to 15 drops to be instilled into the ear  
 as directed.

## LARYNX

- R Tinct. Benzoin. Co. . . . . fl. oz. 1 (28·4 c.c.)  
 Sig.—15 to 30 drops in a jug of hot water for an  
 inhalation.

**PHARYNX**

- R Sod. Bicarb. . . . . gr. 40 (2·4 gm.)  
 Liq. Thymol. Co. . . . . fl. oz. 1 (28·4 c.c.)  
 Glycer. . . . . fl. oz. 1 (28·4 c.c.)

Dilute eight times with water.

Sig.—The throat spray or gargle, to be used as directed.

- R Phenol.  
 Sod. Sulphocarb. . . . .  
 Sod. Bicarb. . . . . āā oz.  $\frac{1}{2}$  (15·5 gm.)  
 Glycer. . . . . fl. oz. 5 (142 c.c.)  
 Liq. Carmin. . . . . ℥ 5 (0·3 c.c.)  
 Aq. Aurant. Flor. . . . . fl. oz. 4 (114 c.c.)

Sig.—Dilute with an equal quantity of water and use  
 as a gargle.

*Mandl's Paint*

- R Iod. . . . . gr. 5 (0·3 gm.)  
 Pot. Iod. . . . . gr. 25 (1·5 gm.)  
 Ol. Menth. Pip. . . . . ℥ 5 (0·3 c.c.)  
 Glycer. . . . . fl. oz. 1 (28·4 c.c.)

Sig.—Use as a paint as directed.

I. S. HALL.

# DISEASES OF THE RESPIRATORY SYSTEM

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## THE PREVENTION OF ACUTE RESPIRATORY DISEASES

*(Coryza, Acute Bronchitis and Broncho-pneumonia)*

**T**HE commonest predisposing causes of the more severe respiratory diseases, such as bronchitis and pneumonia, are coryza and influenza.

This is particularly the case when infection occurs in individuals whose resistance is lowered from any cause. It is for this reason that we believe that in the field of prevention, education of the individual sufferer from the common cold is of prime importance. Infected individuals, particularly during the first twenty-four to forty-eight hours of the disease, should isolate themselves in their homes, or, failing this, refrain from entering places of public entertainment such as cinemas and theatres, etc., where people are crowded together. They should keep as far apart as possible from non-infected persons and should cough and sneeze into a handkerchief with the head averted from neighbours, who should not be submitted to the direct line of fire of infected droplets.

It should be explained to persons in the acute stage of coryza that isolation at home is not merely a social obligation required for the prevention of infection of others, but that rest in a constant temperature is the best means of obtaining a rapid cure and limiting the liability to more serious disease from extension of the inflammation.

During epidemics of acute coryza and influenza, it is particularly important for certain individuals to reduce their chances of infection to a minimum by not entering places where persons are crowded together. This advice applies to elderly and debilitated people in general, sufferers from cardiac and pulmonary disease and, in particular, those with chronic bronchitis, asthma, bronchiectasis and tuberculosis.

In view of the grave complications which may occur in infants and young children, every effort should be made to limit the risks of exposure to infection. Doctors, dentists and nurses have a grave responsibility when suffering from sore throats or colds in the head, and should take particular care to avoid infecting their patients, especially infants and debilitated persons.

Lastly, we would stress the desirability of the early removal to hospitals of infants and young children with measles and whooping-cough. Good nursing and general care, which are not available in many working-class homes, reduce the pulmonary complications which are the principal cause of the mortality.

As conditions exist to-day, the average individual can scarcely hope to avoid infection at some time during the winter months. Every effort should be made to build up the constitution and raise the general resistance of persons who are peculiarly susceptible, or those with chronic organic disease, by giving common-sense advice on the following points:—

1. The avoidance of excessive mental or physical fatigue.

2. The avoidance of undue exposure to wet and cold, by staying indoors when the weather is unseasonable, particularly if cold is combined with fog or mist. This does not mean that fresh air and exercise are harmful—on the contrary, when the weather is suitable, regular open-air exercise, so long as it is within the limits of the patient's tolerance, is one of the most important factors in building up the natural resistance. The beneficial effects of fresh air can be continued at night by insisting that bedroom windows are kept open. In addition, in schools and institutions where the dormitory system is in existence, the beds should be spaced at least 7 ft. apart.

3. The wearing of heavy clothing in the house leads to an unhealthy condition of the skin, an organ which plays a most important part in allowing the patient to adjust himself to changes of temperature and pressure. Light clothes should be worn indoors, with, for outdoor use, an overcoat of a thickness to suit the climatic conditions. The fact is well recognized that although females muffle themselves up much less than males, they are noticeably less susceptible to colds. Wet and therefore cold feet, especially if endured for hours in the office or factory, are a potent factor in lowering the vitality, often with serious consequences. The obvious preventive measure is the use of stout footwear. Health as well as comfort may be dependent on having a dry pair of shoes and stockings available at the place of work.

4. Since chronic irritation of the air passages predisposes to infection, attention should be directed to the irritation produced by an atmosphere of cigarette smoke. In certain cases it may be necessary to prohibit or at least curtail smoking. The individual's occupation should be ascertained. Should it involve exposure to excessive amounts of dust or chemical fumes in the atmosphere, a change of occupation may be necessary.

**Local Measures.**—The nose and throat should be examined for abnormalities which impair the free entry of air and lead to mouth breathing, *e.g.*, deflected septum, polypi, enlarged tonsils and adenoids. Chronic infection of the air sinuses and tonsils, if present, should receive attention, since this may cause a lowering of resistance to the viruses of the common cold and influenza.

Practical experience does not encourage the wearing of masks by healthy individuals as a safeguard against infection. A mask is more likely to be effective in preventing the spread of infection if worn by persons actually suffering from the disease.

Gargles and spraying with mild antiseptics night and morning are believed by many to be of value as a preventive measure. Hydrogen peroxide, glycerin thymol co., etc., are commonly used for this purpose. An atomizer is required when oily solutions are advised. Mild antiseptic solutions, or normal saline, may also be used as a nasal douche. We would remind the reader not to use any forcible measures for the introduction of fluids into the nose (see p. 726). Douching is more effective if reserved for the later stage of coryza, when it will remove any thick secretion obstructing the airway. In our experience, the preventive value of local applications to the nose and throat has been exaggerated. We do not recommend the use of penicillin and sulphathiazole snuffs, penicillin sprays or lozenges in the prophylaxis of coryza or influenza.

**Diet and Tonics.**—In poorly nourished or debilitated patients, dietetic measures are important in building up the resistance. It is seldom that a

diet is deficient in a quantitative sense, since calories can be purchased very cheaply in the form of carbohydrates such as bread and potatoes. The qualitative deficiencies present in the diet of the working classes are mainly in animal proteins, minerals and vitamins. This can very easily be corrected by the ingestion of an extra pint of milk a day and some fresh fruit and green vegetables. Iron, when anæmia is present, and cod-liver oil to increase the intake of vitamins A and D should be prescribed. On the other hand, obesity is a potent factor in lowering the resistance, particularly if the patient is taking a diet deficient in animal proteins, vitamins and minerals. Accordingly, the caloric intake in such individuals must be reduced (see p. 383), while the so-called protective foods must be given in adequate amounts.

**Faulty Posture and Breathing.**—Proper ventilation of the lungs requires efficient and full movements of the diaphragm. This not only empties the lungs of air lying dormant at the bases, but corrects the tendency of the blood to stagnate in the large abdominal veins. Faulty breathing is frequently accompanied by faulty posture, for the correction of which an understanding of the principles of body mechanics, as enunciated by Goldthwaite and Swaim of Boston, is necessary. Drugs are useless for this purpose, and reliance must be placed on special exercises carried out regularly every day. Reference to the section on rheumatic diseases (p. 844) will indicate the great importance of correcting these abnormalities as a means of raising the general resistance.

**Vaccine Therapy.**—No more controversial question exists in medicine than the value of vaccines in the prophylaxis and treatment of disease. In our experience vaccines are rarely useful, and are often harmful when given in the acute stage of any disease. With regard to the prophylaxis of such a condition as the common cold, it is extremely difficult to assess the merits of vaccine therapy because of the wide variation in susceptibility and resistance in different individuals, and in the same individual at different periods. Since it is now established that the infective agent of a common cold is a filterable virus, it seems unlikely that the manifold claims made in the medical press during the past twenty years regarding the value of prophylactic anticatarrhal vaccines can now be maintained. Since the more serious complications such as sinusitis, tracheitis and bronchitis are due to secondary invaders which can be incorporated in a vaccine, the possibility exists, and there is some evidence to support it, that vaccines may prevent or reduce the severity of such complications. For this purpose a mixed stock anti-catarrhal vaccine may be given subcutaneously on three or four occasions at weekly intervals in the late summer or early autumn to individuals susceptible to coryza and its complications. In view of the short period of immunity conferred, the course should be repeated in January or February. The dosage usually recommended is 0.25, 0.5 and 1 c.c. at weekly intervals. If anything more than a mild degree of local or general reaction follows an injection, the dose should not be increased at the next injection, and may possibly have to be reduced. Prophylactic immunization should not be undertaken if coryza is already present, in view of the danger of a serious reaction.

For the prevention or amelioration of recurrent winter cough which so frequently occurs in chronic bronchitis, a mixed catarrhal stock vaccine is frequently employed. Some authorities stress the importance of having

the organisms in the patient's sputum identified and an autogenous vaccine made. There is more to be said for this procedure if a single organism is present in almost pure culture. Whether a stock or autogenous vaccine is employed, it is essential to proceed with great care in regard to the dosage. It is generally agreed that the maximal dose of vaccine should be less than the amount which will produce any general reaction. In view of the great variation in individuals the dosage can be found only by trial and error. Accordingly, it is wise to start with a very small quantity of vaccine, *e.g.*, 0.1 c.c., containing from 1 to 5 million organisms. The subsequent doses should be given at weekly intervals and progressively increased, but always with care to avoid general reactions. By this means the patient's immunity mechanism is believed to be steadily stimulated. Reactions, on the other hand, may induce a state of increased sensitivity to bacterial antigen, and, if severe, may precipitate an acute illness.

## ACUTE CORYZA

*(Acute rhinitis, cold in the head)*

**Definition:** A catarrhal inflammation of the nasopharynx due to a filterable virus; a secondary infection with pyogenic organisms usually follows.

Treatment will be considered under two heads: (1) measures to abort the infection in the early stages and (2) treatment of the established condition.

**Measures to Abort the Infection in the Early Stages.**—When an individual comes home from work with a slight soreness of the throat and stuffiness of the nose, it is sometimes possible to abort the incipient coryza by one or more of the following measures.

He should take a hot bath, followed by a hot drink of lemon or black-currant juice sweetened with sugar, to which 1 oz. of whisky may be added should the patient desire it. Five to ten grains (0.3 to 0.6 gm.) of aspirin and the same quantity of pulv. ipecac. et opii. (Dover's powder) will secure a good night's rest.

For the purpose of shrinking the congested nasal mucous membranes, a 1 per cent. solution of ephedrine in saline, or an oily solution containing some of the essential oils (with or without ephedrine), may be sprayed into the nose through an atomizer (for prescriptions, see p. 773). For acute catarrhal conditions the solution of ephedrine in saline is undoubtedly the best. "Endrine" can be used in an atomizer or 1 to 2 drops can be run into the nose by means of a pipette. Amphetamine produces a rapid but evanescent shrinkage of the mucous membranes and can be purchased in a convenient form of inhaler. Local astringents, since they shrink swollen mucous membranes and thereby clear the exits of the air sinuses, are held to be of value in reducing the risks of sinusitis. Though the claims made by the manufacturers regarding the efficacy of their preparations in aborting the common cold are often exaggerated, there is little doubt that a temporary symptomatic improvement does occur. It is necessary, however, to utter a warning against the excessive use of preparations of this type. If used too frequently the secondary reaction which follows the vasoconstriction may cause a turgescence of the mucous membranes greater than before, and may lead to an increase of inflammation or even necrosis of the epithelium.

Accordingly, local vasoconstriction should not be attempted more than three or four times in the twenty-four hours except in cases of acute infection where the instillation of 1 per cent. ephedrine in saline may be required more frequently in order to prevent obstruction and infection of the nasal sinuses. This preparation has no deleterious effects on ciliated mucous membrane.

Douching with warm normal saline assists in freeing the airway by removing secretions and organisms, although it does not produce such dramatic effects as obtained from vasoconstrictor drugs. It is advisable to run the saline into the nose gently from a pipette, stopping at once if any tendency to swallowing or retching occurs. The nose should not be blown for at least a quarter of an hour after the operation. These instructions are given in order to avoid forcing infected material into the Eustachian tubes.

**Treatment of the Established Condition.**—If the measures already described fail to abort the condition and the patient has reached the acute stage of coryza with profuse rhinorrhœa, the most important question to be decided is whether he should be allowed to go to work or be confined to the house. If fever is present, or if the patient is old or debilitated, or has any coexisting serious organic disease, there can be no doubt about the advisability of remaining in bed. Personally, we advise all sufferers from acute coryza to stay at home, if possible, since we believe that by far the most effective way of obtaining a rapid cure is to remain indoors in an even temperature in a well-ventilated but warm room for twenty-four to forty-eight hours. By this means the liability to the serious sequelæ from extension of the inflammation to the nasal sinuses and the bronchial tree is reduced to a minimum.

Individuals with acute coryza should realize that they are suffering from an infectious disease which they may pass on to others with results which may be disastrous. Hence they have a moral obligation to isolate themselves during the acute infective stage, *i.e.*, during the first twenty-four to forty-eight hours.

It is a time-honoured custom to start the treatment of any acute disease with a purge. Since this question will arise in all the acute respiratory diseases, we propose to discuss it fully now in order to save repetition.

Our own feeling is that the routine administration of calomel or castor oil at the beginning of an illness is to be deprecated, since purging is invariably followed by an upset of the normal rhythm of evacuation, and, if carried too far, has a debilitating effect. Accordingly, if the patient has had a regular daily evacuation of the bowels up to the onset of the illness, we do not advise the administration of an initial purge. If, however, the patient has been constipated for the preceding day or two, an aperient will have to be given. Two to three grains (0.12 to 0.18 gm.) of calomel followed by Epsom salts in the morning has been shown by long clinical experience to achieve a satisfactory evacuation. Calomel, however, does not suit everyone, and it is wise to inquire of the patient which laxative he has found to be most satisfactory. This preparation will cause the least disturbance to the patient, and a double dose will ensure a satisfactory evacuation. Should constipation persist, it is better to rely on small doses of a mild laxative such as senna or cascara at night, followed next morning by an enema. A single evacuation from an enema is less exhausting to a debilitated patient than a series of watery motions resulting from a purgative.

Since acute coryza in the vast majority of cases is a self-limiting disease of short duration, no question arises of supplying a diet which will meet the maintenance caloric requirements. A light, easily digested diet, of the type used in fevers (see p. 4), whose constituents should, within reason, meet with the patient's approval, is all that is required. Fluids should be taken in abundance. The patient should drink daily at least 4 to 6 pints of water, fruit drinks, tea, etc.

*Drugs.*—Provided there are no complications, the only drugs required are 10 gr. (0.6 gm.) of aspirin, which may be taken three or four times a day, and 5 to 10 gr. (0.3 to 0.6 gm.) of pulv. ipecac. et opii. (Dover's powder), taken at night with a hot drink. The sulphonamide drugs are contra-indicated in uncomplicated coryza.

*Local Treatment.*—In our experience the most suitable form of local treatment is the instillation of 1 per cent. ephedrine solution in saline. The inhalation of steam impregnated with Friar's balsam, menthol or eucalyptus is also a useful measure. A jug which will hold approximately 2 pints should be half-filled with water from a kettle that has been "off the boil" for a few minutes, thus reducing the risk of scalding the patient's face or cracking the jug. One teaspoonful of Friar's balsam is added to the hot water for its sedative effect, while the addition of a small crystal of menthol or 5 to 6 drops of oil of eucalyptus will stimulate a freer flow of secretion. The jug is surrounded by a towel whose ends are gathered together to form a funnel through which the patient inhales the vapour. It is advisable to keep the eyes outside the funnel in order to avoid irritation from the medicated steam. When sinusitis is present, the exits from the sinuses may be enlarged and drainage facilitated by shrinking the nasal mucous membrane by the local application of astringents (see p. 773) 10 to 15 minutes before the inhalation of steam. If the nares are blocked by thick viscid secretion, gentle douching with warm normal saline is recommended and should be carried out after the steam inhalation.

We do not advise the use of penicillin sprays or lozenges or penicillin and sulphathiazole snuff for the treatment of coryza. The evidence that they are of value is equivocal and there are dangers of producing a state of "drug fastness" by their use in suboptimal amounts.

*Complications.*—For the treatment of sinusitis, tonsillitis, tracheitis, etc., the reader is referred to the appropriate sections.

## ACUTE BRONCHITIS AND BRONCHO-PNEUMONIA

Acute bronchitis is an acute inflammation of the mucous membrane of the bronchi, which may be mild or intense and may affect the trachea, bronchi or terminal bronchioles. The further down the bronchial tree the inflammation spreads the more serious will be the systemic manifestations. No sharp dividing line exists between tracheitis, bronchitis, capillary bronchitis and broncho-pneumonia.

A primary form of broncho-pneumonia is described in infancy and early childhood, but in the great majority of cases it is secondary to an inflammation of the terminal bronchioles, which leads to small lobular areas of consolidation and collapse, scattered mainly throughout the bases of the lungs. The conditions leading to bronchitis and broncho-pneumonia have



already been discussed in the sections dealing with the prevention of acute respiratory diseases.

Treatment must vary in every case, depending on the severity of the infection and the resistance of the individual.

In mild cases of tracheo-bronchitis in healthy persons, confinement in a warm well-ventilated room at an even temperature for a few days and the administration of a simple cough mixture, if so desired, is all that is required. At the other extreme, some patients with acute bronchitis and broncho-pneumonia may be so seriously ill that they will need the best of nursing and medical treatment if a successful issue is to be obtained.

### GENERAL MEASURES

The patient must be confined to bed in a warm room at a constant temperature of 65° F. It is so essential to conserve the strength of those patients who are seriously ill that they must be relieved of every effort. Skilled nursing, accordingly, is always necessary. Unless this can be afforded, hospital treatment is indicated.

The patient's night-wear should consist of a light woollen vest, a flannel bed-jacket and pyjama trousers. The common mistake of allowing the patient to be covered with several layers of thick heavy clothing is an important factor in inducing restlessness and discomfort, so preventing sleep. Tepid sponging of the whole body, avoiding undue exposure, morning and evening, and of the face and hands on other occasions when the patient feels feverish, is very comforting. If the patient is not debilitated and little or no fever is present, a hot bath may be ordered provided the bathroom is close to the bedroom and the patient returns immediately to bed. The night-wear should be changed at frequent intervals if sweating is present.

A light, easily digested fluid or semi-fluid diet should be ordered (see p. 4). It should be given in small amounts at two-hourly intervals along with a plentiful supply of fluids in the form of weak tea, barley water, fruit juice in water sweetened with glucose, etc. One tumblerful of fluid should be taken at least every two hours during the day.

To prevent intestinal distension, bulk and roughage in the diet should be avoided. A choice should be made from the following articles: milk, which may be citrated by the addition of 2 gr. (0.12 gm.) of sodium citrate to each ounce (28.4 c.c.), milky foods (Benger's, Allenbury's, Ovaltine, etc.), milk puddings, ice-cream, custards, jellies, eggs, broth, gruel and vegetable purées.

In old and debilitated persons the nurse should alter the patient's position in bed from time to time, to prevent him from slipping down into a flat position, since this may increase the difficulty in breathing and the liability to hypostatic congestion. The patient should be permitted to assume the position in bed which he finds most comfortable. In general, this is the inclined position, the patient's back being supported by pillows or a bed-rest and his knees by a bolster placed beneath them. If available, beds specially constructed for the nursing of cardiac and respiratory cases are convenient. The danger of thrombosis of the veins of the lower limbs should be remembered and measures undertaken for its prevention. Active and passive movements and massage of the lower limbs should be regularly carried out.

### SYMPTOMATIC TREATMENT

**Insomnia and Restlessness.**—When the small tubes are affected and the patient is in a weak, toxic condition, it is essential to ensure sufficient sleep. Before resorting to hypnotics, the following measures should be tried. Sponging with tepid water, placing the patient in a comfortable position, rearranging the bedclothes, getting the patient to pass urine and giving 10 gr. (0.6 gm.) of aspirin and a hot lemon drink with or without the addition of whisky are simple measures, which, when given by a skilled nurse, are often sufficient.

The commonest cause of sleeplessness in bronchitis is a distressing, painful cough, in which case the best hypnotic is a sedative linctus (see p. 774). When insomnia is due to the restlessness caused by fever and toxæmia, 10 to 30 gr. (0.6 to 1.8 gm.) of chloral hydrate is an excellent preparation. Should this be unsuccessful the barbiturates may be tried,  $7\frac{1}{2}$  gr. (0.5 gm.) of barbitone soluble or 3 gr. (0.18 gm.) of sodium amytal. Paraldehyde, 2 to 4 drachms (7.2 to 14.4 c.c.) by mouth or 4 to 6 drachms (14.4 to 21.6 c.c.) emulsified in 2 oz. (56.8 c.c.) of saline per rectum, is a safe and good hypnotic. The unpleasant taste may be disguised by taking it with an equal quantity of whisky flavoured with syrup of orange. Unfortunately, whether given by mouth or by rectum, a nauseating smell in the breath may persist for several days. Opium or its alkaloids should be used only if sleep is being prevented by a hacking cough or severe pain in the chest. Its use in full doses is dangerous, if there is much secretion in the lungs or if marked cyanosis is present. This warning is given lest by the stoppage of the cough reflex the bases of the lungs become water-logged with the danger of death from asphyxia. If there is much secretion it is advisable to give  $1\frac{1}{10}$  gr. (0.6 mg.) of atropine sulphate along with not more than  $\frac{1}{8}$  gr. (10 mg.) of morphine or  $1\frac{1}{2}$  gr. (5 mg.) of heroin.

**Delirium.**—A mild degree of delirium is frequently present in pneumonia, the patient suffering from hallucinations and mild confusion. Marked delirium is one of the most serious complications and indicates intense toxæmia and anoxæmia. Treatment of these severe cases is unsatisfactory because the amount of sedative required to control the delirium may produce a fatal issue from depression of the respiratory centre. Oxygen is obviously indicated, although the mask or nasal catheter or even the oxygen tent is often badly tolerated. The patient must be restrained, if necessary by strapping the limbs to the bed. In general, however, reliance has to be placed on hypnotics despite their danger. Morphine is contraindicated. Thirty grains (1.8 gm.) of chloral hydrate or one of the barbiturates, 6 gr. (0.36 gm.) of sodium amytal, may be tried if the patient can be induced to swallow. Otherwise, rectal or parenteral treatment must be employed. Five to eight drachms (18 to 28.8 c.c.) of paraldehyde emulsified in 2 oz. of normal saline may be given per rectum, or 3 gr. (0.18 gm.) of sodium phenobarbitone intramuscularly.

**Cyanosis.**—When broncho-pneumonia is complicated by congestive heart failure the removal of 10 to 20 oz. of blood from a vein (see p. 939) is recommended when cyanosis develops or when the veins of the neck are distended. Venesection is particularly effective in plethoric individuals, with whom, indeed, it may be useful even before the appearance of cyanosis.

The early administration of oxygen in adequate quantities is essential in all persons suffering from capillary bronchitis and broncho-pneumonia with cyanosis (for details, see p. 954).

**Circulatory Failure.**—In patients seriously ill with evidence of a failing circulation, the question of cardio-respiratory stimulants will invariably arise.

Their routine administration is to be deprecated, and the choice of drug must be decided according to the circumstances of each individual case.

**Alcohol.**—Alcohol is used much less frequently to-day than it was thirty years ago. This is certainly due to the fact that in the past it was the practice to starve feverish patients, whereas to-day every effort is made to keep them in caloric equilibrium. As Hutchison says, "We have swung, in fact, from a regimen of starvation mitigated by tipping to one of mild stuffing modified by total abstinence. There can be no doubt that the change is, on the whole, wise, though perhaps it has gone too far."

Brandy or whisky may be used. Good whisky is better than bad brandy. Half to one ounce of spirits three or four times in the twenty-four hours is generally sufficient.

Whisky and brandy are usually considered as stimulants, though, in fact, they are sedatives. Nevertheless, for the following reasons, alcohol is of value, particularly in elderly persons or those accustomed to taking it regularly:—

1. It promotes rest and sleep, and lessens apprehension.
2. It dilates the peripheral blood vessels, inducing diaphoresis and augmenting heat loss.
3. It is a source of energy easily absorbed and, in the quantities indicated above, it is metabolized without risk of cumulative effects.

**Digitalis.**—The routine administration of digitalis in capillary bronchitis and pneumonia is a matter on which acute controversy exists. In febrile conditions accompanied by heart failure and auricular fibrillation, no one doubts its value, but it is certain that in febrile states digitalis will not slow a rapid pulse whose rhythm is regular. Those who prescribe digitalis where the rhythm is regular maintain that it improves the tone of the cardiac muscle and lessens the tendency to cardiac dilatation. Whether it has such an action is disputed both by pharmacologists and physicians. Nevertheless, many experienced physicians believe that elderly people or patients with chronic heart disease benefit from the onset of the illness by the administration of 10 to 15 minims (0.58 to 0.87 c.c.) of tincture of digitalis three times a day. We do not prescribe digitalis as a general routine, but only when the earliest signs of cardiac failure appear, when we prefer to rely on the rapid effect of the intravenous injection of 0.5 mg. digoxin (B. W. & Co.), followed by 0.25 mg. by mouth every six hours. The full effect of the drug can be obtained in a short time by this method.

Other stimulants which require mention are nikethamide, methedrine, leptazol, posterior pituitary extract, adrenaline, strychnine and caffeine. In acute heart failure we believe that nikethamide given in doses of 2 to 4 c.c., intramuscularly or intravenously, is a valuable drug. The dose can be repeated four-hourly if required. When the failure is more peripheral than central, methedrine (B. W. & Co.) may be given parenterally, either intramuscularly (dose 15 to 30 mg. in 1.5 c.c.) or intravenously (dose 10 to 20 mg. in 1 c.c.). The beneficial effects as estimated by the rise in blood pressure occur within 15 minutes and are much more prolonged than when pituitary

extract or adrenaline are used. It is our practice in critical cases, where the circulation is failing, to give alternate injections of nikethamide and methedrine at two-hourly intervals. Strychnine is probably employed more often than any other drug for the treatment of cardiac failure in acute respiratory disease. Strychnine is essentially a respiratory stimulant, and any beneficial effects it can have on the heart must be secondary to an improvement of pulmonary ventilation. In the usual dosage of  $\frac{1}{160}$  gr. (0.6 mg.) subcutaneously, it is of no value at all. When strychnine is considered desirable, at least  $\frac{1}{30}$  gr. (2 mg.) must be given before any result can be expected. The dose may be repeated in four to six hours. Caffeine is widely used and safe, and may be given in the form of caffeine and sodium benzoate, 2 to 5 gr. (0.12 to 0.3 gm.) subcutaneously every four to six hours.

The stimulants mentioned above are in everyday use for the treatment of circulatory failure, but it appears to us that much of the benefit claimed from them is exaggerated, being based on uncritical clinical observation. The circulation fails because of anoxæmia, dehydration and toxæmia. The rational procedure is the prevention or limitation of circulatory failure by the use of oxygen, infusion of glucose saline and the administration of sulphonamides and penicillin. These must, of course, be given sufficiently early and in adequate amounts.

**Dehydration.**—Dehydration is indicated by dryness of the tongue and skin, a low urinary output and a low blood pressure. If the patient is unable to take sufficient liquid by the mouth to restore the tissue fluids, one or two litres of 5 per cent. glucose solution should be given intravenously by the drip method (see p. 930). The intravenous infusion of isotonic fluids is strongly contraindicated in the presence of pulmonary oedema.

**Tympanites.**—Minor degrees of meteorism may occur from the ingestion of excessive quantities or unsuitable articles of food. It is desirable, therefore, to examine the motions for the purpose of correcting the diet. If thick curds are being passed per rectum, the quantity of milk should be reduced, diluted with water and citrated or peptonized. Marked abdominal distension is usually the result of paralysis of the intestinal muscle consequent on toxæmia. For its prevention, early diagnosis is of first importance along with the use of sulphonamides, oxygen and intravenous infusions of glucose saline in adequate quantities.

For its treatment a soft rubber catheter (rectal tube) should be passed and left in position. To induce peristalsis and so to expel the gaseous contents of the bowel, 1 c.c. of pituitrin is injected intramuscularly, the same quantity being repeated one hour later if necessary. Enemata are less effective. Occasionally, meteorism may be relieved by  $\frac{1}{2}$  gr. (7.5 mg.) of calomel every hour, or, alternatively, one fluid drachm (3.6 c.c.) of castor oil every three hours until the bowels move.

**Cough, Spit and Pain in the Chest.**—In the early stages the patient has an irritating non-productive cough, accompanied by pain under the sternum. The objects of treatment are to loosen the sputum, lessen the cough and relieve the discomfort. For these purposes the following measures are indicated:—

**External Measures.**—The room should be well ventilated and a constant temperature maintained around 65° F. A fœtid, stuffy atmosphere is itself a potent factor in maintaining an irritating cough. Moistening the air by steam from a steaming kettle at a distance of several feet from the patient is comforting. The steam may be medicated by the addition to the water

of a few drops of oil of eucalyptus or terebene. The steam tent may be used instead or the steam may be inhaled directly, as already described under the treatment of acute coryza.

For the retrosternal soreness, local applications of heat to the chest are of value. Poultices are usually unsatisfactory. They are messy, smelly and disagreeable when they have cooled and are troublesome to prepare. It is better to use a rubber hot-water bottle, filled to a third of its capacity only to keep it lax and suitably covered with blanket cloth. An electrically warmed pad, when available, is a useful alternative.

*Internal Measures.*—It is traditional for the doctor to prescribe a cough mixture for his patients suffering from bronchitis and pneumonia. Since widely differing opinions are held about the value of cough mixtures, we propose to discuss the matter in some detail. Cough mixtures can be divided into three main groups.

Sedative cough mixtures are prescribed for the purpose of checking a painful non-productive cough which is exhausting the patient and preventing him from resting or sleeping. Opium and its alkaloids, particularly codeine, are of special value for this purpose (see prescriptions, p. 774).

Anti-spasmodic cough mixtures are prescribed for the relief of bronchial spasm, however produced, and are of particular value in bronchial asthma. Adrenaline and ephedrine are very effective. The value of lobelia, stramonium and belladonna in the usual pharmacopœial doses of 10 to 20 minims (0.58 to 1.16 c.c.) of the tincture thrice daily is, however, doubtful.

Expectorant cough mixtures are employed for liquefying viscid bronchial secretions, increasing their flow and facilitating their expulsion. For these purposes the following drugs are frequently employed singly or in combination—ipecacuanha, squill, senega, ammonium carbonate, ammonium chloride and potassium iodide.

While universal agreement exists in regard to the value of sedative and anti-spasmodic cough mixtures in suitable cases, the same cannot be said about expectorant cough mixtures. Accordingly it would appear desirable to consider briefly the evidence on which the claims to their therapeutic value are based. The evidence obtained from experiments on animals such as the rabbit, guinea-pig and cat is conflicting, some workers claiming that the output of bronchial secretion is increased by expectorant drugs, while others state the results are negative. Even if the positive results claimed to occur are accepted, their clinical implications must be interpreted with great caution, because the dosage used in animal experiments was relatively enormous, and if given to man in equivalent dosage based on body-weight would have certainly produced vomiting and possibly serious or even fatal poisoning. It is thus apparent that the clinical value of expectorants can be assessed only by trial in patients. This is notoriously difficult because of the tendency to improvement which occurs spontaneously within a few days in most cases of acute bronchial catarrh and of the fluctuation in the amount of bronchial secretion expectorated from day to day in such chronic conditions as bronchiectasis and chronic bronchitis. The views of generations of experienced physicians must not be lightly dismissed nor, however, must they be implicitly accepted if unsupported by careful measurement and assessment of the quantity and quality of the bronchial secretion expelled before and after the administration of the so-called expectorant drugs.

When such a carefully controlled experiment was undertaken by Alstead it was found that ipecacuanha, ammonium chloride, ammonium carbonate and potassium iodide given in average official doses four times daily after meals produced no effect on sputum output which could not be attributed to spontaneous variations similar to those seen in the control periods. Alstead states that the opinions of patients as to the value of various cough mixtures was found to be wholly unreliable, judging by their assessments of inert substances such as cochineal in water.

The fact that an emetic dose of ipecacuanha taken on a fasting stomach reflexly causes an increase of bronchial secretion, which is removed together with the gastric contents by the violent muscular efforts accompanying vomiting, does not justify the assumption that a small subemetic dose taken on a full stomach will reflexly cause an increase in bronchial secretion. Similarly, the fact that potassium iodide may induce coryza and increased bronchial secretion in people who have an idiosyncrasy to the drug does not prove the value of iodides as expectorants. Nor does the finding of traces of potassium iodide in the sputum within a few minutes of its administration necessarily indicate its value in liquefying or increasing the volume of bronchial secretions. Iodides being readily diffusible, salts can also be found in many other secretions. In other words, there is no pharmacological evidence of the selective excretion of iodides by the bronchial tree.

It will be generally agreed by the unbiassed observer that the therapeutic actions claimed for the expectorant drugs are based mainly on clinical impressions sanctified by tradition and poorly supported by data from experimental work on animals or from properly controlled investigations in man. It is a striking fact that medical and surgical specialists in diseases of the lungs are much more sceptical about the value of expectorant cough mixtures than general practitioners and place little reliance on their employment. Since, however, it must be admitted that their therapeutic value is still debatable, any doctor may prescribe expectorant mixtures if he so desires. (For prescriptions see p. 774.) Patients usually expect a bottle of medicine, and the psychological benefits are undoubted even if the pharmacological effects are dubious. Cough mixtures containing drugs in pharmacopœial doses are harmless to the patient but may be dangerous to the doctor prescribing them if he fails to appreciate this psychological aspect, since by attributing to his skilful prescribing results which may have been otherwise produced, he blunts that critical faculty of judgment on which the sound practice of medicine so largely depends.

The beneficial effects of hot drinks in relieving painful spasm and loosening secretions are not fully realized, and after each dose of a cough mixture a hot lemon drink should be sipped.

The value of inhalations of penicillin sprayed from an atomizer in controlling infections of the bronchial tree and thus facilitating the expulsion of secretion cannot be said to be proved. We believe this method is worthy of trial in the more serious pulmonary infections in which there is a viscid spit (see p. 734).

**Pulmonary Œdema.**—Rarely a condition of bronchorrhœa occurs, as indicated by a profuse expectoration and the presence of bubbling râles scattered throughout the lungs. In severe cases pulmonary œdema may develop, in which case the prognosis is very bad. Pulmonary œdema is a medical emergency requiring prompt treatment. Atropine in doses of  $\frac{1}{8}$  to  $\frac{1}{6}$  gr.

(2.4 to 1.2 mg.) should be injected subcutaneously at once and repeated if necessary at two-hourly intervals. Venesection (10 to 20 oz.) should be carried out and oxygen given continuously by the intranasal route.

Pulmonary oedema occurring in lungs the seat of inflammation responds even less favourably to the injection of atropine sulphate than when the primary cause is left-ventricular heart failure. It is doubtful whether morphia should be given for pulmonary oedema associated with severe respiratory diseases because of its depressant effect on the respiratory centre. If, however, restlessness is marked,  $\frac{1}{8}$  gr. (10 mg.) of morphia may be justified. Oxygen (90 per cent.) should be given continuously through a B.L.B. nasal mask. The intravenous injection of 100 c.c. of 50 per cent. sucrose has been recommended with the object of abstracting fluid from the tissue spaces. Sucrose is stated to be better than glucose because its effect is more lasting. The beneficial effects should appear within an hour.

Dry cupping may also be tried as this reflexly stimulates the capillaries to absorb fluid.

### SPECIFIC THERAPY

Chemotherapy is contraindicated for the treatment of mild cases of tracheo-bronchitis with little systemic disturbance. For capillary bronchitis and broncho-pneumonia, sulphonamide drugs and penicillin are now the most important life-saving measures available. Sulphadiazine, sulphathiazole, sulphamerazine or sulphamezathine should be used in the manner and in dosage detailed on p. 74. The indications for penicillin by injection are discussed on p. 90 and by inhalation in the following section. Penicillin should be given by injection and not by inhalation in broncho-pneumonia.

### INHALATION OF PENICILLIN

Inhalation of penicillin is of value in the treatment of intra-pulmonary sepsis, but certain essentials are necessary for successful treatment. It is essential that the apparatus should be capable of delivering a cloud of penicillin particles sufficiently small to penetrate to the smallest bronchi and alveoli. In order to deliver sufficient penicillin to the patient the flow rate of the machine must be at least 6 litres per minute. Of the machines on the market at the moment the only one which meets this requirement is the Collison inhaler, though improved Phantasol machines will probably soon be available.

The following conditions are benefited by inhalation therapy:—

*Acute Bronchitis.*—Rapid improvement and cure can be expected in the majority of cases.

*Chronic Bronchitis.*—In both purulent and non-purulent types the results are variable. Some cases are much improved, but relapse is usual a few weeks or months after the cessation of treatment.

*Bronchiectasis.*—Inhalations should be given before meals and preceded by postural drainage. Treatment may have to be persisted with for four to six weeks. Such improvement as may occur in chronic cases is, as would be expected, only temporary. Patients with acute exacerbations often respond dramatically, toxæmia lessening and fever settling rapidly.

In *lung abscess* it is of value in sterilizing the bronchial tree, in preventing infection spreading to other parts of the lungs and in preparing the patient for operation. In these cases, though the sputum is often sterile,

the pus from the abscess usually still contains a growth of the causative organism.

When the organisms become scanty as the result of successful treatment, particularly when staphylococci disappear, an overgrowth of *B. coli* often occurs. They are much diminished in number though not eliminated by giving inhalations of sulphacetamide either with the penicillin or at some other time in the day.  $1\frac{1}{2}$  gm. of sulphacetamide by daily inhalation is usually sufficient to control the growth of *B. coli*.

Our practice is to give penicillin in a concentration of 50,000 units to the cubic centimetre, the patient receiving 1 to 2 c.c. four times a day. We have found the daily inhalation of a single large dose of 200,000 to 300,000 units to be much less satisfactory. The patient should be instructed to inhale through the nose and exhale through the mouth, and the penicillin can be given by the Collison oro-nasal mask or by the B.L.B. mask. Bronchial spasm may be relaxed by the inhalation of a solution of 1 in 100 adrenaline, immediately before the inhalation of penicillin.

### CONVALESCENCE

After an acute attack of bronchitis or broncho-pneumonia, it is most desirable that the patient should have a holiday of at least two to four weeks before returning to work, to ensure complete resolution of the diseased process in the lungs. If possible, convalescence should be spent in surroundings where the patient can get sunshine, change of air and scenery and good nourishing food, including plenty of milk. Most hospitals have a convalescent home which is suitable in these respects, while for better-off patients a holiday at the seaside should be ordered. In this country, however, a sheltered inland resort may be more beneficial in winter-time. Care should be taken not to send the patient to a holiday resort at a long distance from his home until he is physically fit for the journey. While no artificial measures are so valuable as exercise in the fresh air along with good food, nevertheless, ultra-violet radiation and tonics (cod-liver oil and vitamin preparations containing vitamins A and D and yeast), while supplemental, should not be omitted.

**Delayed Resolution.**—If resolution has not occurred as judged by clinical and radiological examination, prolonged convalescence is essential. Breathing exercises should be undertaken for five or ten minutes several times daily, followed by postural coughing. The delay in resolution is due to plugging of the smaller bronchi; thus it is doubtful if aspiration of secretion by a bronchoscope, as advocated by some authorities, can be of much benefit. Since, however, it may be difficult to tell whether the obstruction is in one medium-sized bronchus and also the precise nature of the obstruction, bronchoscopy is advised in every case in which resolution is not proceeding satisfactorily within six weeks.

**Pulmonary Fibrosis.**—Post-pneumonic fibrosis usually manifests itself by recurrent attacks of bronchitis, and has been named by some writers "chronic pulmonary catarrh." Bronchiectasis should be excluded in all doubtful cases by means of skiagrams after the introduction of iodized oil. The most important single measure in the prevention and treatment of this condition is prolonged convalescence at a bracing inland or seaside resort. It is a common mistake to send such patients to a convalescent



home for two or three weeks. The practitioner should insist on at least two months of convalescent treatment, which should include good food, cod-liver oil and regular breathing exercises.

For the treatment of fibrosis of the lung in tuberculosis, pneumoconiosis, etc., see appropriate sections.

## CHRONIC BRONCHITIS AND EMPHYSEMA

Treatment will be considered under three headings: (1) correction of factors of ætiological importance; (2) general measures; and (3) local measures.

**Correction of Factors of Ætiological Importance.**—Chronic bronchitis sometimes follows previous attacks of the acute form, sometimes it appears insidiously as a concomitant of organic disease. In elderly patients it may develop without recognizable cause in the form of a chronic cough, worse in winter.

The treatment of chronic bronchitis does not merely consist of prescribing a cough mixture, but entails in the first instance the study of factors which may be of importance in its causation. For example, in a case where it is associated with obesity and cardiac disease, the prescription of a rational diet along with digitalis and the regulation of the patient's activities, mental as well as physical, will prove more useful than any cough mixture.

The patient's occupation should be ascertained, since it may be maintaining or at least aggravating the cough. Each individual case calls for a separate decision. For instance, working in a dust-laden atmosphere may be very deleterious. The remedy may lie in the use of a respirator, or better ventilation in the factory or workshop. Possibly no remedy will be really effective short of a complete change of occupation.

The nose and throat should be carefully examined for abnormalities which by obstructing the airway encourage mouth breathing, and for infected tonsils or accessory sinuses whose secretions may be draining into the bronchial tubes.

Lastly, we would recall the danger of overlooking chronic fibroid phthisis which not infrequently masquerades as chronic bronchitis.

**General Measures.**—These aim at increasing the patient's own power of resistance. Diet is important here, but it must be adjusted to the needs of the individual. In debilitated persons, for example, abundance of butter, cream, milk and bacon will increase the calorific value of the diet, while the overweight person with cardio-renal disease needs the weight-reducing measures outlined on p. 383.

Regular exercise in the fresh air should be prescribed, always within the limits of the patient's tolerance, but during fog and damp weather he should stay indoors. Those who can afford it will derive much benefit from a winter spent at a resort suitably situated with regard to warmth and sunshine. Unfortunately, the French and Italian Rivas can have spells of unpleasant weather in the winter, when they offer no more advantages than more accessible resorts. To be assured of warm weather and sunshine, it may be necessary to go as far as Egypt or the north coast of Africa. Even in these countries serious respiratory infections are liable to develop unless the patient is warned of the treacherous fall in temperature which occurs

suddenly in the late afternoon and takes the necessary precautions. The cost of a long journey with its attendant risks may easily outweigh the benefit obtained, unless the patient is prepared to stay for at least six weeks in the place selected.

A tepid or warm bath, followed by vigorous friction with a rough towel, is an excellent measure for stimulating the skin. This should be followed by breathing exercises (see p. 844). Common-sense advice should be given regarding the deleterious effects of wearing excessively heavy and thick clothes. Footwear should be sufficiently strong in construction to prevent wet feet.

We are satisfied that smoking is a factor of importance in maintaining and augmenting chronic bronchitis, and we have seen much benefit arising in individuals who have taken our advice and given it up. In general, however, this advice will not be accepted *in toto*, in which case the patient may be persuaded to limit himself to a pipe after each meal. The inhalation of cigarette smoke is particularly harmful.

It is unnecessary to draw attention to the effects of excessive quantities of alcohol on the general resistance, but little harm will be done if it is taken in moderate amounts.

Vaccines, either stock or autogenous, are beneficial in a proportion of cases. Great care must be taken in regulating the dosage to avoid reactions which are undoubtedly harmful. The reader is referred to p. 724, where vaccine therapy is discussed in detail.

**Local Measures.**—The principles underlying the prescription of cough mixtures have been fully discussed on p. 732, to which the reader is referred. In particular, we would again draw attention to the need for studying in every case the quantity and character of the sputum and any associated symptoms such as cough, pain, dyspnoea and bronchial spasm.

Inhalations of medicated steam, as already described, are comforting and should not be forgotten.

When the spit is foetid, creosote, 3 drops in capsules or perles, or five drops of terebene on a lump of sugar several times a day, are of value in masking the foetor of the breath and sputum. Further treatment is discussed on p. 734.

Acute exacerbations of bronchitis with fever and constitutional disturbance should be treated with sulphonamides in full doses (see p. 74) or with penicillin by injection or inhalation (see p. 90 and p. 93).

### EMPHYSEMA

Emphysema is a concomitant of chronic bronchitis in a greater or less degree. The condition is incurable, and treatment consists of stopping or limiting the process by treating the bronchitis. Common-sense advice must be given to the patient on how to avoid upper respiratory infection and on how to regulate his life within the limits of his tolerance to effort. Breathing exercises may be tried, but in general will not be found to be so useful as in asthma. They should be combined with a course of massage to the muscles of respiration with the object of increasing their efficiency. Broncho-spasm is not infrequently present even although the physical signs are not obvious. In all cases of emphysema, therefore, the use of antispasmodic drugs, especially ephedrine, in doses of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 32 mg.), should always be tried. A dose of 4 gr. (0.24 gm.) of caffeine citrate or 3 gr. (0.18 gm.) of

theophylline monoethanolamine (Theamin, Lilly) taken before attempting exercise which leads to respiratory distress may be of considerable symptomatic value. In patients with lax and pendulous abdomens a properly fitting corset, by increasing intra-abdominal pressure and thus raising the flattened diaphragms, may be helpful in alleviating dyspnoea. In the late stages of emphysema, cardiac failure may supervene. Suitable measures for its treatment will be found in the section devoted to diseases of the heart.

## LOBAR PNEUMONIA

Although the specific treatment of lobar pneumonia by means of sulphonamides and penicillin constitutes a major advance, good nursing under the best conditions still plays an extremely important part in bringing the disease to a successful conclusion.

If the patient's home conditions are poor or overcrowded, hospitalization should be recommended. Removal to an institution should take place in the early stage of the disease, and under no condition must he be allowed to walk a single step as this may induce a collapse. A stretcher and ambulance must be employed. When the home circumstances are satisfactory the patient may be treated at home. Adequate nursing and the use of a bedroom with plenty of fresh air and freedom from disturbance by other members of the household are essential.

**General measures** with regard to *nursing, fresh air, position of the patient in bed, diet, care of the bowels, etc.*, and the symptomatic treatment of *circulatory failure, pulmonary oedema, cyanosis, cough, tympanites, insomnia, restlessness, delirium, etc.*, have been fully described in the section devoted to acute bronchitis and broncho-pneumonia (p. 727). These are equally applicable in lobar pneumonia, and hence it is only necessary to refer briefly to certain additional points before dealing in detail with specific therapy.

Lobar pneumonia is a sharp intense infection, from which the patient generally dies or recovers within a few days. Accordingly, it is unnecessary to attempt by dietetic measures to maintain the patient in metabolic equilibrium, as is so important in long-continuing fevers. Nevertheless, the daily caloric requirements may be as high as 3,000 to 4,000 calories when the temperature continues around 104° F. It is considered helpful to conserve the patient's strength and prevent dehydration by ensuring an intake of at least 2,000 calories daily. This can be done by the use of small two-hourly feeds of the articles mentioned on p. 728, with intervening drinks of water or fruit juice sweetened with glucose or lactose. Sleep is of such value to the patient with pneumonia that it should never be broken for the purpose of giving feeds or drinks, making examinations or undertaking procedures such as changing the linen, washing the patient, etc. Visitors should be excluded or severely limited, although due consideration should be given to individual circumstances.

Reference must be made to the use of expectorant cough mixtures in lobar pneumonia. In our opinion they are of no more value than in bronchitis (see p. 732) and we do not advocate their employment.

**Pain and Restlessness.**—*Morphia.*—Severe pain from pleurisy is present in the majority of cases of pneumonia at the beginning of the illness. It leads to much distress, restlessness and insomnia and to shallow breathing which increases the liability to anoxæmia. In our opinion morphia is

indicated if relief is not obtained by the local application of heat (see p. 732), or strapping on the chest (see below), or sedative drugs such as chloral hydrate or aspirin. We consider morphia is of great value in obtaining some hours of rest and sleep, and we use it if necessary during the first two or three days of the illness. One-sixth of a grain (10 mg.) should be given subcutaneously in the evening, and the dose may be repeated in two hours if necessary. Some physicians prefer  $\frac{1}{2}$  gr. (5 mg.) of heroin hydrochloride in the belief that it is a less potent respiratory depressant and tends to cause less intestinal distension. In the later stages of the disease morphia has to be given with great caution. It is contraindicated if marked cyanosis or much secretion in the lungs is present. The last twenty years have seen a considerable change of opinion in favour of the use of morphia in pneumonia. A study of the recent writings of the English authorities leads us to believe that the views expressed above are generally accepted.

*Strapping.*—Fixation of the hemithorax with strips of adhesive tape relieves pain by diminishing movement of the inflamed pleural surfaces on each other. If strapping is to be effective, careful attention must be given to the following details. The tape should be 3 in. wide and should extend to the unaffected side at least 4 in. beyond the middle line, both in front and behind. While a single strip over the lower ribs may be sufficient to relieve pain in some cases, in others three pieces may be required. The upper two strips cross in the axilla, passing above and below the breast, while the remaining strip is used to fix the free margin of the ribs. If hair is present it should be removed by shaving. The strips of plaster should be placed in position during full expiration. Strapping the chest on the lines indicated above does not interfere with physical examination or counter-irritation, should this be considered necessary.

### SPECIFIC THERAPY

Prior to 1938 the only form of specific therapy available was the parenteral administration of concentrated refined antipneumococcal serum. With the discovery of the antipneumococcal effects of the sulphonamide drugs the treatment of pneumonia has been revolutionized and serum therapy has been relegated to the background. Sulphonamide and serum therapy both produce in approximately 80 to 90 per cent. of cases a critical fall in temperature within forty-eight hours, and their influence on mortality rates and on the incidence of complications is approximately the same. Antipneumococcal serum is type specific, and the difficulties and delay in determining the type of the infecting pneumococcus, the fact that it must be given intravenously and the risk of anaphylactic reactions have led to its use being abandoned.

*Sulphonamides.*—Although the treatment of pneumonia has been revolutionized by the introduction of the sulphonamide drugs, it is necessary to emphasize the fact that even with early and adequate treatment there still remains a high fatality rate. Anderson's studies in Glasgow (1943) show that the death rate in sulphonamide treated cases is 12 per cent. and 31 per cent. in type II and type III pneumococcal cases respectively, and 26 per cent. in patients of 41 years or over, the figure rising to 47 per cent. if bacteriæmia is present. Moreover, the serious complications of delayed resolution occurred in 13 per cent. of the total series, whereas the percentage was doubled in patients over 41 or in those with bacteriæmia. The high loss

of life in patients at a time when their responsibilities to the State and their families are at their greatest indicates the danger of complacency and suggests the need for further intensive research for new and more effective drugs. The recent introduction of penicillin may solve some of these problems.

The sulphonamide drugs used for the treatment of pneumonia are sulphathiazole, sulphadiazine, sulphamerazine and sulphamezathine. All four are approximately equally effective in controlling pneumococcal infections. Nausea, vomiting and mental depression are produced so much more frequently by sulphapyridine that the drug should no longer be used. The initial dose recommended is 3 to 4 gm. (6 to 8 tablets) repeated in four hours. Thereafter 1 gm. is given every four hours until crisis or lysis has occurred and continued thereafter for at least forty-eight hours. On the average a total of 30 gm. is required and the minimum period of treatment should be five days. If the patient is seriously ill or unable to retain the tablets because of vomiting, soluthiazole (May & Baker) should be administered intravenously or intramuscularly. It is well tolerated but not suited for subcutaneous use. The drug is a neutral soluble sulphathiazole derivative and the initial adult dose recommended is 15 to 25 c.c., corresponding to 3 to 5 grammes of sulphathiazole. For full details regarding dosage, reactions, methods of administration, etc., see p. 74.

**Penicillin.**—In the average case of lobar pneumonia and mild cases of broncho-pneumonia the first line of attack is the administration of one of the sulphonamide drugs. Under certain conditions sulphonamides are contraindicated, when penicillin should be given intramuscularly according to the instructions on p. 90. Sulphonamide therapy is contraindicated:—

- (1) When there is a clear history of serious toxic reaction following previous administration, *e.g.*, agranulocytosis, hæmolytic anæmia, exfoliative dermatitis, etc.
- (2) Advanced renal disease, especially with nitrogen retention, and severe hepatitis.
- (3) When there has been no response to sulphonamide therapy within 2 to 3 days. In such cases the infecting organism may be resistant to sulphonamide. The drug should be discontinued and penicillin administered if specific therapy is still indicated. At this stage, however, the practitioner would be well advised to review the diagnosis of pneumonia and consider the possibilities of pulmonary abscess, empyema, carcinoma of the lung, tuberculosis, etc.

Combined therapy with sulphonamides and penicillin is indicated under the following conditions:—

- (a) Seriously ill patients with lobar pneumonia, especially if bacteraemia is present; (b) pneumonia caused by the streptococcus, the staphylococcus or Friedlander's bacillus; (c) patients seriously ill with broncho-pneumonia, especially infants and elderly persons.

## PRIMARY ATYPICAL PNEUMONIA

The disease is characterized by a gradual or sudden onset. The most striking feature is the paucity of physical signs in the lungs as compared with the degree of radiological change. The course is benign, usually ending in complete recovery. In the absence of an epidemic and the availability

of radiological help and facilities for leucocyte counts, an accurate diagnosis in the early stage may be impossible. No drug has been known to have any specific influence on the course of the disease, and failure to respond to sulphonamide or penicillin therapy constitutes a diagnostic test of some importance. The pleuritic pain or intense headaches which may characterize the early stages of the illness call for the use of analgesics.

## PLEURISY

The symptomatic treatment of pleurisy is discussed on p. 143. Otherwise its treatment is that of the underlying disease.

## ACUTE EMPYEMA

Empyema may complicate any type of pneumonia and at any age. When it is suspected an exploratory puncture should be carried out in order to ascertain the character of the pus, which should be examined bacteriologically. In addition, an X-ray film should be taken in bed as it provides valuable information concerning the position and size of the effusion.

The sulphonamide treatment of established empyema seldom yields dramatic results, but may be worthy of trial when the infecting agent is penicillin resistant. Sulphonamides should be given in the dosage indicated on p. 74. Surgical drainage will have to be undertaken at the appropriate time (see below).

The introduction of penicillin into the pleural cavity has proved to be by far the most effective method of controlling infection in all cases of empyema in which the organism is penicillin sensitive. For this purpose from 100,000 to 200,000 units should be injected into the pleural cavity every forty-eight hours following the aspiration of the purulent exudate. Toxæmia is usually maximal in the initial stages when the effusion is turbid and loculation has not taken place. The introduction of penicillin at this stage will cause rapid sterilization of the exudate and a dramatic improvement in the clinical state of the patient. Where the exudate when first discovered is already frank pus, the same technique of aspiration followed by injection of penicillin should be carried out, and sterilization of the pleural contents can be confidently expected within a few days. In addition, however, it will be necessary to secure effective drainage and removal of clots and fibrinous deposits by undertaking rib resection on the lines discussed below. The treatment of such cases by aspiration and penicillin alone is not recommended. Experience has shown that without the addition of free drainage gross pleural thickening results with consequent serious interference with pulmonary function.

Intrapleural penicillin has been successfully used for eradicating secondary infection in tuberculous pleural effusion and for sterilizing extrapleural collections of pus occurring in wounds of the chest wall or after such operations as thoracoplasty. When empyema coexists with continuing pulmonary suppuration due to penicillin sensitive organisms which cannot be controlled by sulphonamide drugs, the systemic administration of penicillin on the lines described on p. 90 must be given coincidentally with the intrapleural injection. It should be noted that there is evidence to suggest

that the inflamed pleural membrane is more permeable to penicillin given parenterally than is the normal pleura.

The appropriate time for and the method of drainage of empyema is governed by the age and general condition of the patient, the extent of the empyema and the infecting agent.

The ordinary (pneumococcal) type of empyema in *adults* usually develops after the crisis of lobar pneumonia, when the respiratory reserve has increased. The pus is thick and is usually localized to the lower and posterior part of the pleural cavity, and the surrounding lung being often adherent to the chest wall. Therefore there is no risk in performing open drainage, which is more effective and certain than other methods. This should be delayed for the few days required to sterilize the effusion by penicillin injection. Drainage should be done by rib resection at the most dependent part of the cavity. Coagula should be removed. The drainage tube should be of wide bore. If it is deemed advisable to secure closed drainage, a long rubber tube must be used, the end being under water in a bottle beneath the bed.

The streptococcal type of empyema may not differ materially from the pneumococcal and may be treated on the same principles. But when, as is common in broncho-pneumonia, the effusion develops in great bulk while the patient is still ill with cyanosis and dyspnoea, open drainage would—in the absence of pleural adhesions—reduce the respiratory reserve still further and prove hazardous. Therefore the toxæmia and the pressure within the thorax should be relieved by repeated frequent and slow aspiration followed by the injection of penicillin. Sometimes, though it must not be relied upon, no further operation is required. Usually when the patient's condition has improved and the lung has secured adhesion to the chest wall with consequent stabilization of the mediastinum, open drainage should be carried out on the same lines as for pneumococcal empyema.

**Empyema in Children.**—In children over five years the treatment of empyema need not differ in its essentials from that in adults. Very frequently closed drainage suffices, but in a proportion of cases it fails and open drainage is ultimately required. Open drainage should never be employed in infants and children under three. It has a much higher death-rate than closed drainage. Closed drainage is almost always sufficient. It should be performed under local anæsthesia.

**Post-operative Management of Empyema.**—In cases in which the purulent discharge remains persistently thick and is not diminishing satisfactorily it is an advantage to irrigate the pleural cavity regularly when the patient is strong enough to tolerate the procedure. Warm saline should be used at first, later an antiseptic solution—such as weak eusol (half eusol, half water)—is preferable, as it helps to dissolve fibrin. The solution should be kept from strong light in a dark bottle. The patient should be so placed that the opening in the chest is uppermost and the cavity is completely filled so that all surfaces are cleansed. If a broncho-pleural fistula is present, however, lavage of the pleural cavity should be avoided.

Recovery is accelerated if the patient is nursed in the open air. Breathing exercises should be started as soon as possible in order to promote expansion of the lung. Active inspiratory exercises are of the greatest value; they require the supervision of a trained physiotherapist, who should pay attention to the maintenance of good posture since scoliosis is liable to occur in cases of chronic empyema.

The progress of lung expansion and diminution in size of the empyema cavity should be estimated periodically by skiagrams, preferably taken anteroposteriorly and laterally. In no circumstances should the drainage tube be removed so long as any significant cavity remains; failure to observe this rule is very common and is the usual cause of recurrence of infection and chronicity of the empyema.

## SPONTANEOUS PNEUMOTHORAX

Pulmonary tuberculosis is a common cause of spontaneous pneumothorax, and routine radiological examination suggests that lesser degrees of pneumothorax are not infrequent and often pass unnoticed. In rare instances it is the first evidence of pulmonary tuberculosis.

Till recent times tuberculosis was considered the almost invariable cause of spontaneous pneumothorax. It is now recognized, however, that when *spontaneous pneumothorax occurs in an apparently healthy person* it is more often due to some non-tuberculous defect in the alveoli or the pleura, such as an emphysematous bulla, or a direct tear of the pleura from traction by adhesions. Sometimes the pneumothorax recurs at varying intervals, and in some instances is bilateral or alternating. It is so seldom complicated by effusion that a simple origin may be inferred.

The escape of air into the pleural cavity in a tuberculous patient may result from softening of superficial tuberculous foci, rupture of a cavity or the dragging effect of adhesions. If the opening in the pleura is oblique or valvular, a serious rise of intrapleural pressure may occur (tension pneumothorax). The escape of infective material usually results in pyopneumothorax (see below).

In a well-marked case of spontaneous pneumothorax there is usually sudden and severe pain in the chest and urgent dyspnoea and cyanosis. In the more severe cases hasty relief is necessary if fatal asphyxia is to be averted.

An X-ray examination should be carried out in order to ascertain the degree of pneumothorax and the presence of such complicating features as effusion and mediastinal displacement. Spontaneous pneumothorax may create considerable shock, alarm and anxiety, and morphia is required for the control of these symptoms.

In many cases the lung quickly re-expands, and this should be awaited if there is only slight distress. If there is urgent dyspnoea, and especially if the heart is much displaced, the intrapleural tension should be relieved immediately. In an emergency the insertion of an aspirating needle into the pleural cavity is sufficient for decompression. If the opening in the lung is valvular and/or symptoms recur, the needle should be left in place and connected by rubber tubing to a bottle of antiseptic beneath the bed (water-sealed intercostal drainage). This improvised water valve allows air to escape from, but not to re-enter, the chest. Later, if necessary, further air can be withdrawn by means of an artificial pneumothorax apparatus.

A very full and careful examination should be carried out to exclude the possibility of pulmonary tuberculosis. The milder cases should be treated by expectant measures. Urgent cases should be treated on the lines laid down above.



When a pneumothorax recurs, as it may do, on several occasions, it is advisable to attempt to obliterate the pleural space. Various methods have been tried in the past, such as the insufflation of sterile talcum powder containing 2 per cent. iodine and the injection of 5 c.c. of the patient's own blood. These methods were uncertain in their results and rarely led to the formation of firm adhesions. They have been replaced by intrapleural injections—after removal of most of the air—of 5-10 minims of a 10 per cent. solution of silver nitrate. The injection may have to be repeated, and as it always gives rise to a painful febrile reaction and an effusion which may have to be aspirated under X-ray control, it should only be done in hospital by those experienced in the method.

Should the above measures fail, surgical interference offers the only hope of relief.

**Pyopneumothorax.**—The majority of cases of pyopneumothorax result from an effusion of fluid into a pneumothorax—often artificially induced—associated with tuberculous disease in the lung. In a proportion of cases of non-tuberculous empyemata, air enters the pleural cavity by bronchial fistula. This calls for no special treatment other than that of empyema as described on p. 741.

Following spontaneous pneumothorax of tuberculous origin an effusion develops in a large proportion of cases. At first the fluid is clear and tubercle bacilli are few in number, but there is a special tendency for the infection to progress so that the effusion becomes purulent—pyopneumothorax. Not infrequently a superadded pyogenic infection occurs or, still more serious, the pus may reach the surface or rupture into the large bronchi via a fistula.

The prognosis is always bad, more especially if the infection occurs during the advanced stages of the disease. If the pyopneumothorax complicates early disease of the lung, and especially if the other lung is healthy, active measures should be adopted before toxæmia undermines the patient's strength. For treatment see p. 135.

## HÆMOTHORAX

According to Price Thomas hæmorthorax is by far the commonest complication in chest injuries, for it may be associated with any of the various types of injury produced by blast or crushing in addition to penetrating and perforating wounds. Price Thomas reports an incidence of 70 per cent. of hæmorthorax in a series of 750 cases of chest injuries of all types. Where the hæmorthorax is simple, *i.e.*, not associated with bleeding from injury to the lung, chest wall or diaphragm, treatment by repeated aspiration will procure rapid and complete resolution in the majority of cases. Where the hæmorthorax is complicated by injury to adjacent structures, special surgical measures will be required. Blood in the pleural cavity remains fluid in over 90 per cent. of cases of hæmorthorax, and hence can be aspirated. When clotting takes place, operation must be undertaken for the removal of clot since otherwise the lung will fail to re-expand completely. In approximately one-third of cases with hæmorthorax, infection occurs. When this can be controlled by penicillin injected into the pleural cavity, aspiration alone, repeated at suitable intervals, may lead to complete cure. In other cases, especially when infection and clotting co-exist or when such complications

as a sucking chest wall wound or a bronchopleural fistula are present, special surgical measures will be required.

If the hæmorrhage is a slow one as from the lung, the blood should not be removed for twenty-four hours since the increased intrapleural pressure may seal off the bleeding point. In addition, recently extruded blood has bactericidal properties because of its content of antibodies, leucocytes and macrophages. Within twenty-four hours such properties are largely lost and thereafter the blood becomes a favourable medium for bacterial growth. Later still the blood acts as an irritant to the pleural membranes and an outpouring of fluid results. If this is left *in situ* fibrin formation and other undesirable sequelæ follow.

When the hæmothorax is moderate in extent and the contained blood is fluid, simple aspiration of the pleural contents on several occasions may secure complete expansion of the lung.

Price Thomas and Cleland claim excellent results in the treatment of clotted and infected hæmothorax by a series of measures which include sterilization of the pleural contents with penicillin followed by clot removal by thoracotomy and decortication of the lung. Re-expansion of the lung is secured by active suction procured by joining the drainage tubes in the pleural cavity to an electric suction pump. By these means the authors claim early and complete obliteration of the pleural space, which is the single most important consideration in the prevention and elimination of pleural sepsis.

Penicillin may be given when a sterile hæmothorax is proved to be present by aspiration, with the object of preventing subsequent infection. It should always be given where sepsis of the chest wall or pulmonary infection complicate hæmothorax, as under such circumstances the liability of the hæmothorax to become infected is greatly increased. Penicillin treatment of infected hæmothorax is as valuable as in empyema. Such general considerations as bacteriological proof of the sensitivity of the infecting organism to penicillin, the dosage of penicillin and the method of introducing it into the pleural cavity have been dealt with in the section on empyema and are equally applicable to hæmothorax. The greatest care must be taken when aspirating the pleural contents and when injecting penicillin, not to introduce infection from without, especially infection with gram-negative organisms which are penicillin resistant. All apparatus must be boiled before use and the operation should be carried out with the same rigid attention to aseptic technique as is demanded in the case of laparotomy.

## BRONCHIECTASIS

There are wide variations in the clinical picture of bronchiectasis. The patient may complain only of recurrent cough, or repeated hæmoptysis (bronchiectasis hæmorrhagica sicca) or the classical picture of chronic ill-health, toxæmia, foetid sputum and clubbing of the fingers may be present. There is, in addition, a large intermediate group in which health is not impaired for a great many years despite the expectoration of large amounts of sputum. The type, stage and localization of the disease, as well as the age, social circumstances and general health of the patient are factors which must be taken into consideration in determining the most suitable method of treatment.

### PROPHYLAXIS

A history of one or more attacks of capillary bronchitis or broncho-pneumonia, usually in childhood, is of such frequent occurrence as to suggest that a failure to obtain complete resolution of the inflammatory process is a factor of great ætiological importance in bronchiectasis. Accordingly, the family doctor should realize the essential need for thorough treatment in the acute stage of broncho-pneumonia by the measures outlined on p. 727, and the need for preventing the child from resuming its ordinary activities until every method has been tried to promote complete resolution. Such measures include a good diet, fresh air, a holiday at a convalescent home and breathing exercises carried out regularly two or three times a day. If atelectasis is present and fails to respond to the above measures, the use of a bronchoscope may be necessary to remove inspissated mucus or pus causing bronchial obstruction (see p. 735).

The bronchoscope should also be employed for the treatment of lobar collapse due to obstruction of a bronchus by a foreign body. The latter should be removed as soon as possible because of the liability of the bronchial tree to infection and dilatation.

Since persistent infection of the nasal sinuses is one of the most important causes of initiating and maintaining infection of the bronchial tree, this possible source of infection must be looked for and if present treated in every case.

### MEDICAL TREATMENT

Although the disease may be a slowly progressive one, and medical treatment is only palliative, it can do much for the improvement of the general health, the reduction of toxæmia if present, the promotion of effective drainage of the bronchiectatic cavities and the reduction of the fœtor of the sputum. Even in cases selected for surgical treatment, a pre-operative course of treatment on medical lines is always indicated.

**General Health.**—The measures for the raising of the general resistance advocated for the prophylaxis of acute respiratory disease (p. 722) and the treatment of chronic bronchitis (p. 736) are equally applicable in bronchiectasis, since patients suffering from this disease are particularly liable to attacks of acute respiratory infection. Fresh air and exercise are the best tonics, but attention should be paid to climate, good food, suitable clothing, etc. Cod-liver oil may be prescribed during the winter. Iron is indicated if anæmia is present (see p. 470). Every case should be examined for chronic infection of the nasal sinuses, a frequent concomitant of bronchiectasis. Infected tonsils and adenoids and septic teeth should be removed. Patients with pyrexia will require rest in bed, and if possible should be nursed in the open air under sanatorium conditions.

**Postural Drainage.**—The most important medical measure for improving the general health and reducing the quantity and fœtor of the sputum is the emptying of the dilated bronchi and cavities by postural drainage. If regularly and efficiently carried out, the sputum may be reduced from several ounces to a trace in a few weeks. The resulting improvement in the general health is often remarkable.

**Intermittent Postural Drainage.**—This is carried out by instructing the patient to lean over the edge of the bed. The head should be well below the

level of the body, which is supported by placing the hands on the floor so that the bases of the lungs are uppermost. A basin is placed on the floor to catch the expectoration and the vomit should this occur. This posture should be adopted two or three times a day before meals for a period of ten to fifteen minutes. We would again emphasize the fact that to obtain satisfactory results from postural drainage, it must be carried out persistently and with attention to detail.

*Continuous Postural Drainage.*—In patients with excessive expectoration, particularly if toxic manifestations are present, who fail to respond to intermittent postural drainage, it is advisable to arrange for continuous postural drainage. This means that the patient must be kept in bed for several weeks until the quantity of sputum expectorated has been reduced to a minimum. The position the patient should adopt will depend on the site of the pulmonary lesions. The posterior bronchi of the lower lobes are most frequently affected in bronchiectasis, and when the disease is situated in this region, the patient should lie prone (*i.e.*, face downward) with the head supported by one pillow and the foot of the bed raised to a height of about 12 in. A special postural drainage bed may be used in which the frame is hinged across the middle so that the centre of the bed can be raised to varying heights. Such a bed may be improvised by the use of a Bradford frame, the most suitable angle of inclination being between 20 and 30 degrees. When the disease is localized in other sites, appropriate postures should be adopted (see p. 750). At the beginning of postural treatment an increase in the amount of sputum usually results, but once drainage is established a gradual diminution occurs. Most patients at first will be unable to tolerate more than five or ten minutes three times a day in the appropriate position. After a few days, drainage may be maintained for a large part of the day and night. During the first few days a slight rise in temperature, along with an increase in toxæmia, may occur. The liability to hæmoptysis is slightly increased, but large hæmorrhages sufficient to endanger life are very rare. Severe reactions or hæmorrhage necessitate the cessation of postural drainage, which may be started again cautiously a few days later. The strain of coughing is very exhausting to patients acutely ill or debilitated by fever and toxæmia. In such cases postural treatment should be discontinued if the exhaustion produced more than counterbalances the effects of the removal of sputum. When the sputum has been reduced to a constant minimum quantity, continuous drainage should be replaced by intermittent postural drainage.

*Bronchoscopic Drainage.*—In certain cases, when there is thick and tenacious purulent material in the cavities or obstruction caused by swelling of the mucous membrane of the bronchi, aspiration and sometimes dilatation through a bronchoscope often results in the establishment of free drainage. The procedure may have to be repeated several times, but should be abandoned as soon as adequate drainage can be secured. Bronchoscopic drainage immediately prior to the operation of lobectomy is invaluable and should be performed in all cases where there is purulent expectoration. Repeated lavage of the infected cavities through a bronchoscope with normal saline and mild antiseptics has not been of much value.

*Drugs.*—The intratracheal injection through a laryngeal cannula of oily solutions containing mild antiseptics such as gomenol, 5 per cent., or menthol, 5 per cent., in olive oil, has been advocated for the purposes of disinfecting

the bronchial tree, but the results have been disappointing. To aid the removal of pus an alkaline mixture followed by a hot drink will be found useful (see p. 774). Inhalations of steam medicated with tinct. benzoin. co. (one teaspoonful to 1 pint of hot water) are also helpful. In general, opiates are dangerous and contraindicated. If the cough is exhausting the patient, the use of a sedative linctus may be unavoidable, and if possible it should be reserved for securing sleep at night. When acute febrile exacerbations occur, sulphonamide and parenteral penicillin therapy (see p. 90) is of great value in controlling the infection.

The inhalation of penicillin by means of a Collison inhaler or a hand vaporizer (for details see p. 93) is useful in temporarily reducing the quantity and fœtor of the sputum, particularly in the treatment of acute febrile exacerbations. In addition, penicillin inhalation is a form of treatment which can be undertaken in the home by patients who develop acute respiratory tract infection and who are known to have pre-existing pulmonary disease.

**Hæmoptysis.**—Hæmoptysis is a fairly common symptom in bronchiectasis. The hæmorrhages are usually small and of little significance; large hæmorrhages, so profuse as to endanger life, are rare. The symptomatic treatment is similar to that adopted in hæmoptysis from other causes such as tuberculosis (see p. 140). In bronchiectasis, however, when the bleeding is a possible source of danger to life, operative treatment may be indicated if the case fulfils the criteria discussed below.

### SURGICAL MEASURES

**Lobectomy.**—Lobectomy is the only operation which offers complete cure in bronchiectasis, but it is not an operation which should be undertaken lightly. A decision to advise lobectomy calls for sound clinical judgment, the co-operation of physician and surgeon, and the consideration of a number of factors. The service of a surgeon specially trained in surgery of the chest is essential, since in inexperienced hands the operation carries with it a high mortality. Unfortunately, the prolonged training required by the thoracic surgeon has led to the supply falling short of the demand. The exact site and extent of the disease should be carefully determined by lipiodol examination. The middle lobe on the right side and the lingular lobe on the left side are said to be involved in a large proportion of cases. The disease is easily overlooked if the bronchial tree in these sites is not well filled with lipiodol. In general, only cases in which the disease is entirely or mainly confined to one lobe are suitable for lobectomy. Elderly people do not stand the operation well, and one should hesitate to advise lobectomy if the patient is over the age of forty. Children, on the other hand, are much better risks than adults. The general condition of the patient, as shown by the degree of toxæmia and the amount of sputum, is a factor which demands careful consideration. The risks of operation vary directly with the amount of sepsis present. In cases of chronic ill-health and marked toxæmia in which numerous adhesions may be present, the operative mortality may be high. On the other hand, in young adults and children suffering either from dry hæmorrhagic bronchiectasis or bronchiectasis with expectoration but with no toxæmia, the operative mortality varies from 2 to 17 per cent. in different hands.

It must be remembered, however, that persons who suffer from bronchiectasis may remain in good health and live as normal members of society for many years. Lobectomy should be considered if efficient medical treatment fails to reduce symptoms to tolerable mildness, if there are recurrent febrile attacks, or if some major complication such as lung abscess or empyema has already occurred. Wide clinical experience is necessary in the assessment of these factors in order to steer a middle course between premature operation and undue delay until gross infection has occurred which so greatly increases operative mortality. No hard-and-fast rules can be laid down, and each case should be considered on its own merits. For instance, one would have more hesitation in advising lobectomy in the case of the breadwinner of a large family than in a young unmarried woman in whom the constant expectoration of foul pus makes her a social outcast, or in whom life becomes unbearable because of the mental anxiety resulting from repeated hæmorrhages. The social circumstances are frequently of paramount importance in influencing the decision in favour of operation.

**Pre-operative Measures.**—The operative risks can be reduced considerably if efficient medical treatment is carried out prior to the operation. This includes improvement of the general health, eradication of septic foci in the upper respiratory tract and reduction of the amount of sputum by postural treatment and bronchoscopic drainage. Tuberculous disease should be carefully excluded. Where possible, operation should be undertaken in summer rather than in winter, and a pre-operative course of sulphonamide or penicillin treatment should be given.

Thoracoplasty, phrenic evulsion and artificial pneumothorax have all been tried in the treatment of bronchiectasis with disappointing and sometimes disastrous results, and are accordingly contraindicated.

## ABSCESS OF THE LUNG

Abscess of the lung may arise without apparent cause, may complicate pneumonia or bronchial carcinoma, or may follow surgical operation (especially on the nose, mouth or throat) or the inhalation of a foreign body, etc.

From the point of view of prophylaxis, the prevention and treatment of post-operative complications are of importance (see p. 751). It is not sufficiently realized that every patient who is about to undergo a major surgical operation under general anaesthesia should first have any sepsis in the mouth and throat treated. Since abscess of the lung may follow dental extraction, the removal at one operation of a large number of septic teeth under general anaesthesia is to be deprecated.

In the early stages medical treatment is indicated, since complete spontaneous cure not infrequently occurs by rupture of the abscess into a bronchus with expectoration of the pus. The treatment of abscess of the lung in each individual case varies with the cause and duration of the abscess, the site and extent of the lesion, the general condition of the patient and whether rupture into a bronchus with adequate drainage has occurred.

The exact site of the abscess should be determined at the earliest possible moment by means of antero-posterior and lateral skiagrams, and if neces-

sary by the introduction of lipiodol. Exploratory puncture of the chest with a needle in order to locate the abscess should not be attempted on account of the risks of infecting the pleural cavity.

**Medical Measures.**—Measures should be taken to improve the general health by diet, tonics and good nursing (see p. 728). It is of advantage to nurse the patient in the open air if the weather is good and the patient is not too enfeebled. Every effort should be made to promote effective expectoration of the pus, since this is the fundamental principle of medical treatment. For this purpose *continuous postural drainage* carried out on the lines described on p. 747 should be instituted. When the abscess is situated in the upper zone the patient should be supported in the sitting position by pillows. When the abscess is situated in the middle zone the patient should be treated lying supine on his side, or prone, according to the position of the lesion as demonstrated by a lateral skiagram of the chest. For a lesion in the lower zone, the foot of the bed is raised about 12 in., and the patient lies supine, in the lateral position or prone, depending on whether the abscess occupies the anterior, lateral or posterior region of the lower lobe.

Inhalations of medicated steam are soothing, and will often help to loosen viscid sputum. The cough is often very irritating and exhausting, especially in debilitated patients. As far as possible the use of opiates should be avoided, but the practitioner may be forced to prescribe a sedative linctus (see p. 774) to secure rest and sleep. Penicillin by inhalation or parenterally may be of great value in the treatment of lung abscess, and should always be given a full trial (see p. 734). A course of sulphonamide for 7 to 10 days may be given concurrently. The practitioner must realize, however, that penicillin and sulphonamide therapy cannot replace the other important medical and surgical measures.

The treatment of foetid sputum, a frequent concomitant of lung abscess, containing large numbers of Vincent's organisms (spirochætes and fusiform bacilli), has been discussed on p. 737.

**Bronchoscopy.**—If the presence of a foreign body or bronchial carcinoma is suspected, bronchoscopy should be performed as soon as possible. Bronchoscopy is indicated in all cases which are not responding to postural drainage, or in which the general condition is deteriorating, or where skiagrams reveal progressive enlargement of the cavity. Where poor drainage is due to the obstruction caused by granulation tissue, swollen mucosa or inspissated pus, aspiration through a bronchoscope may result in the establishment of free drainage. But, if the abscess is draining freely into a bronchus, bronchoscopy is unlikely to give better results than efficient postural drainage.

**Surgical Measures.**—Surgical measures are chiefly reserved for cases in which the abscess is single and situated near the periphery of the lung. They should be considered when, after three to four weeks of adequate medical treatment, effective drainage has not been secured, or the patient is losing ground as evidenced by intractable cough, loss of weight and toxæmia, or if skiagrams show incomplete emptying of the cavity. No hard-and-fast rules can be laid down, and the decision, if and when to advise operation, is often exceedingly difficult. The operation usually indicated is thoracotomy, which consists in the majority of cases of a two-stage procedure.

(1) Resection of segments of rib overlying the abscess which has been

accurately located clinically and radiologically. This alone is enough to produce pleural adhesions but it is customary to close the wound over a gauze mop, either dry or soaked in iodine, applied to the outer surface of the parietal pleura. (2) Incision of both layers of pleura and the thin layer of compressed lung overlying the abscess. The cavity is emptied by suction and loosely packed with gauze.

Pneumonectomy and lobectomy are serious operations but may be required occasionally when surgical drainage has failed to produce obliteration of the cavity.

Thoracoplasty has not justified the expectations of those who have advocated it, and cannot be recommended.

## POST-OPERATIVE PULMONARY COMPLICATIONS

The treatment of such complications as bronchitis, pneumonia, abscess of the lung and empyema have been dealt with elsewhere. Subphrenic abscess calls for surgical measures.

### ATELECTASIS

Atelectasis is one of the commonest post-operative pulmonary complications. It may be patchy or lobular, or may involve an entire lobe (massive collapse). The onset is usually sudden and occurs within the first twenty-four to forty-eight hours after the operation, particularly an abdominal one. The immediate cause of the collapse is obstruction of a bronchus by inspissated mucus or purulent secretion. Numerous factors predispose to retention of bronchial secretions, but if steps are taken to correct these beforehand, the liability to post-operative collapse will be greatly reduced.

**Prophylaxis.**—*Before Operation.*—When any respiratory infection is present, such as bronchitis or even a cold in the head, the risk of atelectasis is increased, and major operations should always be postponed if possible. Heavy smokers are particularly liable to post-operative pulmonary complications. Accordingly, it may be advisable to stop or reduce smoking for one or two weeks prior to operation.

If postponement is possible for a month or longer, individuals with deformities of the chest or faulty methods of breathing should be given a course of remedial exercises before operation.

Secretions are apt to stagnate in the bronchi of elderly patients, particularly if they are obese and flabby. Before operating on these patients measures should be taken to reduce their weight (see p. 383), and gas and oxygen anæsthesia is to be preferred to ether at operation. A pre-operative course of penicillin by inhalation (see p. 93) combined with postural coughing may be of great advantage in elderly patients with chronic bronchitis.

*After Operation.*—CO<sub>2</sub> is the natural stimulant of the respiratory centre. For increasing the depth of respiration in individuals who breathe weakly after severe operations the inhalation through a nasal catheter of 5 per cent. CO<sub>2</sub> in oxygen has been found of great value. It may be given for half-hour



periods every two or three hours for the first twenty-four to forty-eight hours after the operation.

After all major operations the position of the patient should be changed three or four times during the day. The nurse should remove the pillows, place the patient on his side, and, while supporting the abdomen with the hand, encourage him to cough. Constricting bandages around the lower part of the chest and abdomen interfere with expansion of the lower lobes and should never be allowed. Flatulent distension has a similar effect and should be corrected. The suppression of the cough, for example, by pain in the wound, is a potent factor in the production of atelectasis. Small doses of morphine, not more than  $\frac{1}{8}$  gr. (10 mg.), will relieve the pain sufficiently to enable the patient to breathe more freely and to cough without discomfort. Large doses of morphine are contraindicated since they depress the cough reflex. Atropine should not be used after operation as it tends to increase the tenacity of the mucus in the bronchial tubes, thus rendering its expectoration more difficult.

**Treatment.**—At the onset of a severe case of atelectasis, the usual remedies for shock will be necessary (see p. 681). If cyanosis and dyspnoea are present, oxygen should be given continuously (see p. 954).

Many patients will respond to simple measures, such as encouragement to cough, frequent changes in position, and the administration of adrenaline and ephedrine if bronchial spasm is present.

Morphine in small doses of  $\frac{1}{8}$  gr. (10 mg.) should be used only if the patient is suffering from severe pain which cannot be relieved by the milder sedative drugs such as aspirin, phenacetin and codeine, and by the local application of heat (see p. 732).

Oxygen with 5 per cent. carbon dioxide will promote deep breathing and may help to dislodge the obstructions in the bronchi.

If the above measures fail and collapse of the lung still persists at the end of twenty-four hours, bronchoscopy should be seriously considered with a view to removing the obstructing secretions.

Artificial pneumothorax often provides dramatic relief in cases in which there is extensive collapse of the lung with symptoms of a high negative intrapleural pressure and in which bronchoscopic drainage is either not available or has been unsuccessful. Enough air should be introduced into the affected side to correct the very high negative intrapleural pressure. Pain due to drag on the mediastinum is reduced, and the suction traction of the chest wall upon the collapsed lung is abolished, so diminishing the development of bronchiectatic dilatation and giving the patient back his ability to cough. In consequence there is less likelihood of sputum being sucked into the smaller bronchi and bronchioles.

### PULMONARY EMBOLISM AND INFARCTION

In the majority of cases the pathological process which may end in pulmonary embolism begins in the veins of the muscles of the calf. Prophylaxis depends on a correct appreciation of the factors influencing venous thrombosis. It is now generally agreed that anticoagulant drugs are as valuable in pulmonary embolism as they are in the prevention and treatment of venous thrombosis. Accordingly it has been decided to include the treatment of pulmonary embolism and infarction in the section devoted to diseases of the blood vessels (see p. 695).

## INTRATHORACIC NEW GROWTHS

## MALIGNANT TUMOURS

**Bronchial Carcinoma.**—The radical cure of cancer of the lung by the complete extirpation of the affected lung is rarely possible, since by the time the patient presents himself for examination, metastasis to the bronchial glands and elsewhere has nearly always occurred. With improved methods of diagnosis, and of surgical technique, it is reasonable to hope that there will be an increase in the number of cases suitable for operation.

The great majority of cases will have to be treated on medical lines. Radium needles or radon seeds introduced directly into the growth through a bronchoscope have given disappointing results. Deep X-ray therapy may cause shrinkage of the growth, and may be useful in the later stages of the disease in alleviating distressing symptoms, such as pain, stridor and œdema. Prolongation of life, however, can only be expected in a very small proportion of cases.

Sooner or later measures will have to be taken for the relief of breathlessness, pain and cough. Increasing doses of Liquor Morph. Hydrochlor. should be given three or four times a day. In the late stages, morphine should be given freely by hypodermic injection. Heroin is preferred by some, and the combination of morphine and cocaine, of each  $\frac{1}{4}$  gr. (16 mg.), has been recommended.

In many instances there is bound to be difficulty in determining whether the growth is amenable to operation or not. Assistance in this respect may be obtained by thoracotomy, a procedure which should be undertaken more often than it is, as it is not a more dangerous operation than exploratory laparotomy. Even thoracotomy, however, is contraindicated if the following conditions are present:—

(1) Extension of the growth in a main bronchus to within less than an inch from the bifurcation of the trachea; (2) signs of mediastinal invasion, *e.g.*, phrenic paralysis, paralysis of vocal cord, etc.; (3) pleural effusion, either serofibrinous or hæmorrhagic; (4) metastases in other organs.

**Lymphosarcoma and Hodgkin's Disease**, affecting the mediastinal glands, often respond in a remarkable manner to deep X-ray therapy. Life may be prolonged for one or two years, but unfortunately these tumours always recur, and the disease is sooner or later fatal. For the general treatment of these diseases see p. 516.

## NON-MALIGNANT TUMOURS

The prognosis in innocent tumours and cysts of the lung and mediastinum is better than in malignant cases. Provided the patient survives the operation, complete cure may be expected. The decision to recommend operation may be very difficult. If the tumour is discovered accidentally, it is advisable to watch the rate of growth by means of serial skiagrams. Operation should be performed only if the tumour is increasing in size, or if pressure signs develop. In the majority of cases, however, when the patient consults his doctor signs of pressure are manifest. In such cases, operation should be carried out, if, after careful consideration of the size and position of the tumour and the general condition of the patient, reasonable prospects of success may be expected. Bronchial adenomata may have local invasive

properties and recent experience suggests that under these conditions lobectomy is indicated. Otherwise treatment must be on symptomatic lines. It may be possible to remove such tumours as adenomata and fibromata of the larger bronchi by means of the bronchoscope.

## **SPECIFIC NON-TUBERCULOUS INFECTION OF THE LUNG**

Pulmonary lesions may be produced by syphilis, fungus infections (actinomycosis, aspergillosis etc.) and hydatid disease. For their treatment, see appropriate sections.

## **ACUTE OEDEMA OF THE LUNGS**

In Pneumonia, see p. 733. In Cardiac Disease, see p. 660.

## **ASTHMA**

Definition. A spasmodic contraction of the bronchial muscles causing paroxysmal dyspnoea which is chiefly expiratory in character.

Treatment will be considered under two headings: (1) treatment of the acute attack; (2) the management of the asthmatic state.

### **TREATMENT OF THE ACUTE ATTACK**

If the attack of asthma is of sufficient severity to require the attendance of a doctor, the following measures should be instituted. The patient should be sent to bed and propped up in the position which he finds most comfortable. The most effective way of relieving bronchial spasm is to stimulate the sympathetic nervous system. For this purpose a subcutaneous injection of adrenaline hydrochloride, 1 : 1,000 solution, should be employed. Adrenaline loses its potency with keeping, particularly if exposed to the air or to sunlight. It should therefore be kept in tinted rubber-capped bottles in the dark and even then should be renewed every three months. The earlier in the attack that adrenaline is given, the more effective will be its action. Thus a small dose such as 3 to 5 minims (0.17 to 0.29 c.c.), if given at the onset of wheezing, may completely abort the attack, while twice this quantity may be unsuccessful in bringing relief to a patient in whom the paroxysm has lasted for an hour or two. It is for this reason that we believe that patients whose paroxysms are not controlled by the measures described in the section devoted to the management of the asthmatic state, should be instructed how to inject themselves with adrenaline. Should the initial dose fail to control the attack, the dose may be repeated at half-hour intervals. There is no evidence, as far as we know, that any harmful effects result from the frequent injection of small amounts of adrenaline, even when asthma and hypertension coexist. In some cases, however, when many daily injections are given over a period of weeks, the individual appears to acquire a partial tolerance to the drug as shown by the poor effects produced even when large doses are given. Adrenaline should always be injected very slowly by the subcutaneous route. After introducing the needle under the skin and before injecting the drug, the piston of the syringe should be slightly withdrawn to make sure that the needle is not in a small vein, since the

intravenous injection of adrenaline causes unpleasant reactions, *e.g.*, tremor, bursting headache, faintness, palpitation or even collapse.

Counter-irritation to the chest is soothing to the patient and in some cases undoubtedly helps to relieve bronchial spasm. For this purpose one or other of the following may be tried—a linseed poultice, with or without the addition of mustard, a kaolin poultice, dry cupping the back of the chest, the application of hot turpentine stupes or a mustard leaf to the sternum.

Should three or four injections of adrenaline at half-hourly intervals fail to control the paroxysm of asthma, posterior pituitary extract either alone or combined with adrenaline (asthmolysin) in a dose of  $\frac{1}{2}$  to 1 c.c. should be given subcutaneously. Some cases which have failed to respond to adrenaline are amenable to this combined therapy.

In a very small proportion of cases of great severity the measures already described fail to bring relief. The patient may be described as being in "status asthmaticus." To break this state, it will be necessary to introduce antispasmodic drugs under the skin almost continuously. A 1 c.c. syringe filled with adrenaline should be strapped to the skin of the forearm after introducing the needle under the skin. One minim (0.06 c.c.) should be injected every 30 to 60 seconds until relief has been obtained. As much as 120 minims (6.9 c.c.) may be required in a severe case. Thereafter, to prevent a relapse, it is advisable to give 1 to 2 minims (0.06 to 0.12 c.c.) every quarter of an hour for the next hour, twice in the second hour, and once an hour for another two or three hours; or alternatively an intramuscular injection of adrenaline in oil may be given. The protective effect of the oil causes the adrenaline to be slowly absorbed and prolongs the physiological action of the drug. Each cubic centimetre contains the equivalent of 30 minims (1.7 c.c.) of the 1 in 1,000 solution of adrenaline chloride, and the initial hypodermic dose in adults should be 0.5 c.c. A suitable preparation is produced by Parke, Davis & Co. A similar preparation which allows of the slow liberation of adrenaline is Hyperduric Adrenaline, in which the drug is in the form of a salt of mucic acid. The usual adult dose is 0.5 to 1 c.c. hypodermically. These measures will be found to be effective in controlling the majority of cases of "status asthmaticus." In our experience the psychological factor is of predominant importance in "status asthmaticus" and the resistance to adrenaline treatment may be so marked that even the heroic measures advised above may be ineffective. In that case a preparation of theophylline should be given intravenously, *e.g.*, theophylline with ethylene diamine (Aminophylline) or theophylline monæthanolamine (Theamin, Lilly). In both cases the dose is 0.25 gm. in 10 c.c. of water. The intravenous injection should be made very slowly and may be repeated at hourly or two-hourly intervals if necessary.

In addition, the sedative effect of one of the following drugs is of benefit: phenobarbitonum soluble, gr. iii (0.18 gm.), intramuscularly, or paraldehyde, 4 to 6 drachms (14.4 to 21.6 c.c.), per rectum. Morphine is in general contra-indicated in asthma because of the liability to habit formation. Its use involves a grave danger of asphyxia because the large amounts of mucus which may be secreted after the spasm has been relieved will not be removed if the cough reflex has been abolished.

When the paroxysm has been relieved by one or other of these measures, the patient should be given an antispasmodic mixture (see Appendix) and

$\frac{1}{2}$  gr. (0.03 gm.) of ephedrine hydrochloride every six hours. If the attack has been severe and prolonged the patient will be exhausted and should be advised to stay in bed for twenty-four hours or longer. He should take a light, easily digested diet in small quantities at two-hourly intervals, and large amounts of fluid of which fruit juice sweetened with glucose should form a part.

### THE MANAGEMENT OF THE ASTHMATIC STATE

"Many physicians feel their responsibility ended after the control of the acute paroxysm" (Coca).

This attitude cannot be too strongly deprecated to-day in view of the advance of knowledge in regard to the factors which underlie the asthmatic constitution. Every effort must be made (1) to ascertain the immediate exciting cause of the paroxysm; (2) to determine the ætiological factors; (3) to institute therapeutic measures to prevent recurrence or, if this is impossible, to diminish the number and severity of the attacks.

The management of the asthmatic state does not consist in giving an antispasmodic mixture, but entails the taking of a careful clinical history and the making of a complete investigation of all systems. Apart from certain general measures, treatment therefore varies in every case since it will depend on the recognition of the causative factors and the assessment of their relative importance. Hence it can be understood why the claims of certain enthusiasts, that their own particular remedy is a cure for all cases of asthma, are totally unconvincing. Asthma resembles the chronic rheumatic diseases, since in both there exists a constitutional basis which can be affected by a wide variety of exciting agents.

While for clearness of description the ætiological factors must be separately considered, in practice they frequently occur in combination. Hence treatment is often unsuccessful because one factor has received exclusive attention. The importance of the combination of factors is well exemplified by the story of Trousseau. He found that contact with stable dust brought on mild asthma. If, however, he lost his temper with his coachman in the stable where he was in contact with dust, an extremely severe paroxysm of asthma occurred, though anger when he was out driving with his coachman did not induce asthma.

### THE PSYCHOLOGICAL FACTOR

In our experience the most important single factor in asthma is the psychological one. The typical asthmatic is a highly strung, over-anxious, emotional and intelligent person, whose broncho-constrictor centre in the medulla is in a peculiarly irritable condition, being easily influenced by many types of minor stimuli. If we accept the constitutional basis of asthma as being of great importance, we can understand the danger of using the word "cure," since the removal of some abnormality in the nose or the correction of some dietary indiscretion may temporarily relieve the asthma but will leave unchanged the underlying constitutional basis. It is not surprising, therefore, that asthma may again occur when the broncho-constrictor centre is irritated by other stimuli.

It should be noted that the broncho-constrictor centre, which for con-

stitutional reasons is excessively irritable, will react to psychological stimuli of a degree insufficient to have any effect on normal individuals.

It is only within the last few years that the real importance of the psychological factor in asthma has been fully realized. It is the influence of this elusive factor which makes it so difficult to assess the value of any one therapeutic measure. It has long been known that the majority of cases of asthma cease having attacks on entering a hospital ward and often promptly relapse on returning home. The enthusiastic believers in allergy would suggest that the results depend on the removal of the patient from contact with some sensitizing allergen. We believe that in the majority of cases the results are effected by the psychological influence of white-coated doctors and efficient sisters, which gives the patient a hope that something definite is going to be done to improve his condition. In addition, he is transferred to a tranquil environment from one which may be keeping him in a state of nervous tension. The patient's skin reactions may have been positive to dust, feathers, etc., before he entered hospital and will continue to be positive while he is free from asthma in the hospital ward, even though he is sleeping peacefully on a feather pillow. Any treatment involving injections or special manipulations is calculated to inspire confidence in the patient. We, like others, have obtained excellent results in the management of the asthmatic state by injections of distilled water. Since 50 to 60 per cent. of all asthmatics can be improved by a simple antispasmodic mixture and cheerful encouragement by the family doctor, it follows that the claims made for many forms of treatment commonly employed to-day must be accepted with due reserve.

The following case histories are given with the object of illustrating the psychological factor in asthma:—

Case 1. Mrs A., an asthmatic of long standing, had severe attacks periodically. She had lived in the same house for many years. No evidence of allergy was obtained from the clinical history or from skin tests. Her married life had always been unhappy owing to her belief in her inferior social status to her husband. Her sexual life had also been unsatisfactory, although she was the mother of two healthy daughters. A careful analysis of her asthmatic attacks indicated a close association between them and her fear and loathing of her husband. During his absence abroad her asthma quietened down to a mild chronic condition, but anything which brought his presence back to her mind would start a paroxysm, *e.g.*, a conversation with a friend, or reading in a newspaper about his career. The receipt of any letter from him, particularly if it contained any suggestion that he would be coming home on leave, was sufficient to induce a severe attack of asthma, which lasted for several days despite the repeated injection of adrenaline. All efforts at curing the patient have failed, as she will neither accept the situation nor agree to a divorce. Possibly if the psychological aspect had been treated many years previously, results would have been different.

Case 2. A boy aged sixteen, the son of brilliant parents, had had periodic attacks of severe asthma since the age of six. He had eczema in infancy and there was a family history of asthma on his father's side. Skin tests were positive to horse and cat hair, dust and pollen, but negative to all ingestants tested. He had received many kinds of treatment, including non-specific desensitization. His feather pillow had been replaced by one

of sorbo rubber. Periodic attacks of asthma continued just the same. Our analysis of the events immediately preceding his attacks made it clear that anything which induced a state of nervous tension would precipitate an attack. Recently the boy's mother telephoned one of us that he had severe asthma. Inquiry elicited the information that he had been sitting examinations for the preceding three days. An assurance that the attack would immediately subside without any treatment when the results of the examinations were announced, particularly if he had done well, was justified by its immediate cessation on the following day, when the boy was given first-class honours. It is difficult to know to what degree the conscious or unconscious mind was responsible for the attack. The state of nervous tension induced by the examinations could not be avoided by this brilliant youth. On the other hand, the occurrence of asthma at the time of the examinations would be a good excuse if he failed to do well, while if he were successful the accomplishment would be all the more creditable, in view of his physical incapacity. Some two weeks after the examination, when the boy was entirely free from asthma, we repeated his skin tests and found them triple positive to the above-mentioned inhalants. At the same time, tests performed on his three brothers and sisters who were non-asthmatics were negative. The clinical history of eczema and the family history of asthma, together with the positive skin tests, suggest an undoubted allergic factor. Nevertheless, the boy is free from asthma for months on end, despite the presence of cats in the house, or even when he is sleeping on feather pillows. If an allergic factor in this case is the cause of the asthma, it would appear to operate only or chiefly when a state of nervous tension is induced by psychological causes. Concentration on treatment of the allergic factor without correcting the underlying psychological factor is in our experience the principal reason why disappointing results are so frequently obtained in the treatment of asthma.

Case 3. A boy of ten had had asthma for several years. Skin tests were strongly positive to dust, horse hair and feathers. A history of eczema during infancy was obtained. His father wished to know if asthma was an infectious disease, because his other son, aged eight, suddenly started to have asthma. No evidence of an allergic basis was found in the younger child, and inquiry suggested that the asthma was induced in order to receive the favours (sweets, petting by the mother and leave from school) which the elder brother obtained when he had asthma. The position was explained to the child, and suitable advice given to the parents. The child ceased having attacks, and has remained well ever since.

**Assessment of the Psychological Factor.**—For the assessment of the importance of the psychological factor, information regarding the following points must be obtained : (1) personal relations with family and friends; (2) occupation and relations with employer; (3) financial circumstances; and (4) the patient's opinion regarding his state of health, *e.g.*, the fear of disease.

Strauss suggests that help may be obtained by attempting to get an answer to the following ten questions:—

1. Does the patient volunteer the information that he is, generally speaking, "nervy" apart from his asthma?
2. Does he state that excitement or emotion of any kind precipitates an attack?

3. Does he habitually live under conditions involving excessive worry or emotional strain and stress?
4. Is he temperamentally a person who finds it difficult to adapt to his social environment?
5. Is his libidinal life reasonably and legitimately satisfied or satisfiable—judging by superficial standards only?
6. Was he considered to be nervous as a child?
7. Are there any obvious pointers to determinant “complexes” in the psychoanalytical sense?
8. Is a crudely purposive (unconscious) factor detectable and probably a link in the causal chain?
9. Does the patient superficially impress the investigator as being “neurotic” or well balanced?
10. Is the family history “neuropathic”?

Lastly, we agree with Halliday that it is highly important for the doctor to make full inquiries into the following three points:—

1. What kind of person is this? Is he over-aggressive, emotionally unstable, shy and seclusive, etc.?
2. Why did he take ill when he did? Inquiries should be made with regard to the mode of behaviour and psychological factors operating at or before the time of the *first* attack of asthma.
3. What is the person getting at?—*i.e.*, for what end or purpose is this behaviour? An attack of asthma may enable a person to attain what he desires or to avoid something which is unpleasant.

Should the above investigations reveal a psychological element of importance, much can be done by the intelligent practitioner to improve matters. This is particularly the case in children.

*Children.*—The situation must be explained to the mother, so that her natural desire to protect the child may not defeat its own object by inducing a state of nervous tension. Often the mother herself is in a state of nervous tension over some personal problem which is unconsciously transmitted to the child. This aspect is often not realized, and successful results may not be obtained in the treatment of the child if the psychological factor in the parents is neglected. Over-anxiety of the mother leads to pampering the child and making him wear excessive clothing. This must be corrected. There must be no suggestion that he is a delicate child and different from other children, and he must be induced to play with them in order to gain confidence. He must not be withdrawn from school for mild attacks so that he does not use his asthma as a means of avoiding his responsibilities. If the father has adopted a domineering attitude, this must cease. It is important to get the school-teacher to co-operate in these efforts.

Should the family doctor fail to obtain satisfactory results either because of his lack of experience or personality, or because of his inability to obtain the parents' co-operation, the child should be referred to a child-guidance clinic where expert psychological treatment will be available and where organized play therapy is being regularly carried out.

*Adults.*—A different method must be adopted for treating the psychological element in adults.



Careful questioning will frequently reveal a state of mental conflict or anxiety in the patient, consequent on unhappy relations between husband and wife, parents and children, employers and employees, etc. Any cause of anxiety, however, may start an asthmatic attack. For instance one of our patients, who had been instructed to inject himself with adrenaline, told us that on one occasion he was unable to lay hands on his syringe. The terror induced by the mere thought that he had lost his syringe was sufficient to induce a paroxysm of asthma. In other cases, the attack of asthma is used by the patient as a means of escape from performing duties which he finds to be unpleasant, or for the acquisition of sympathy. The family doctor, by the use of explanation and persuasion, can play an important part in relieving the mental conflict or the anxiety states. The mere unburdening of the patient's troubles, followed by a kindly and simple explanation by the doctor of their effect in the production of asthma, is not infrequently sufficient to relieve nervous tension and to produce improvement. In some cases, however, the psychological factor is so complex and so deeply ingrained that it is necessary to refer the patient to a psychologist.

### THE ALLERGIC FACTOR

A state of inherited hypersensitiveness to foreign substances is commonly present in asthma. The sensitizing agent is usually a protein, although occasionally it may be a drug, *e.g.*, aspirin. The assessment of this factor may be difficult, since sensitivity to a substance may vary from time to time for reasons not clearly understood.

In investigating the allergic factor it is essential to obtain a careful history of how and when the original attack of asthma commenced. In general, it may be said that the earlier in life asthma commences the more likely will an allergic factor be found. This probability is increased by the coexistence of eczema, urticaria, prurigo, hay fever or migraine, or a family history of allergy.

The allergen may be absorbed by ingestion or inhalation. The alimentary route is of particular importance in infancy. The commonest foods causing asthma in order of frequency are wheat, egg, milk, chocolate, beans, potatoes, pig products and beef.

In childhood and early adult life, inhalants are of great ætiological importance. The chief inhalants are animal emanations, such as horse dander and feathers, house dust moulds, pollens and orris root, which is so frequently used in face powders. In middle age and late life a history of a lung infection so frequently precedes the original asthmatic attack as to suggest bacterial allergy.

Although the taking of a careful history regarding an allergic factor is of the utmost importance, we would utter a warning against the doctor accepting the patient's statement too easily. Again and again we have had patients who claimed that certain articles of food or some animal emanation produced an asthmatic attack, and yet, when the supposedly offending article was brought into contact with the patient in a disguised form, no asthma resulted. Such experiences suggest that the patient's deductions are often at fault in assessing the part played by any factor in starting an asthmatic attack. In other cases the asthma results from psychological causes, as exemplified by the story of the patient who believed that her

asthma was due to emanations from roses and immediately had an asthmatic attack at the sight of an artificial rose.

Despite these experiences, if the history and skin tests are positive, we recommend that contact with the causative allergen should be avoided or reduced to a minimum, because, although it may not induce an attack in hospital, it may do so in the patient's home if accompanied by a state of nervous tension or anxiety. In addition to taking a careful history it may be necessary to make certain tests for ascertaining sensitivity. For this purpose, solutions of the common inhalants and ingestants can be obtained from leading manufacturers, such as Bencards.

*Intradermal Test.*—The most satisfactory test is made by introducing 0.01 c.c. of the solutions of extracts to be tested into the skin of the volar surface of the forearm. A control injection of carbol-saline is also made. A positive reaction is recognized by the appearance within ten to fifteen minutes of a wheal of at least 5 mm. in diameter. Pseudopodial extensions from the wheal indicate definite sensitivity.

*Scratch Test.*—Another method of skin testing is to place the solution of the extract on the skin, which is scarified through the drop with a needle.

*Interpretation of Skin Tests.*—The interpretation and the clinical significance of the skin tests is far from easy. Thus a patient may give a history of allergy to a certain substance and the skin test may be negative, or more frequently a positive test may be found in the absence of a suggestive clinical history. Again, in our experience, multiple sensitivity is present rather than sensitivity to a single allergen. Lastly, a positive skin test to a solution of house dust is so commonly present in asthmatics that its significance is difficult to assess, particularly since a similar reaction not infrequently occurs in normal persons without asthma. From what has been said, it is clear that the results obtained from skin testing are often unsatisfactory and many physicians have accordingly given them up. We believe, however, that they are of value in a proportion of cases both for the purpose of recognizing and confirming sensitivity and for helping to eliminate the allergic factor in cases which we believe to be purely psychological. Some of our most intractable cases of asthma belong to this category and have negative skin tests.

*Avoidance of the Offending Substance.*—When the clinical history and skin tests indicate that the sensitizing agent is an ingestant or an inhalant, measures should be instituted which will enable the patient, if possible, to avoid contact with it.

*Ingestants.*—If the allergen is some uncommon foodstuff such as strawberries, pork or shell-fish, its recognition is usually easy and its elimination from the diet may produce dramatic results. If, on the other hand, the allergen is a common foodstuff such as wheat, egg or milk, both recognition and avoidance will be difficult because these articles appear on the table in various disguises. To identify the offending substance elimination diets must be used. The bowels are emptied by calomel and Epsom salts, and the patient is placed on a simple basic diet. This diet should consist of one or two articles of food to which the patient is not sensitive. For this purpose orange juice or a milk diet (provided the patient is not sensitive to milk) will be found satisfactory. The patient remains on this basic diet for three days. Thereafter another article of food is added to the diet on each successive day until the offending foodstuff is discovered by the occurrence of

asthma, or reactions resembling the symptoms of the disease under investigation. The offending article can then be eliminated from the diet. When complete elimination is not practicable, marked reduction in the quantity of the allergen in the diet may be sufficient to produce an improvement.

**Inhalants.**—If feathers or horse dander have been definitely inculcated from the clinical history and from the presence of strongly positive skin tests, feathers in pillows and quilts should be replaced by the best Java kapok. Horse-hair mattresses should be covered with rubber sheeting or replaced by the sorbo rubber mattress as supplied by the Dunlop Rubber Company. Chairs and sofas stuffed with horse hair should be replaced by articles of furniture stuffed with kapok. Owing to the expense involved these changes should only be advised if the asthma is not controlled by the other measures described for the management of the asthmatic state, nor should a too optimistic attitude be adopted since in our experience the results are not infrequently disappointing.

A dusty atmosphere undoubtedly predisposes to attacks of asthma, but whether this is due to a specific sensitivity to the dust, or to mechanical irritation of the asthmagenic area in the nose, we are not prepared to say. In either case, the less the patient comes in contact with a dusty atmosphere the better. Accordingly, the minimum of furniture should be kept in the bedroom and a vacuum cleaner should be used for removing dust from the floor, crevices and ledges.

If the patient is sensitive to orris root, then face powders must be prohibited or special preparations free from orris root used. These may be obtained from any chemist (Queen products).

Lastly, sensitization may occur to inhalants with which the patient comes in contact during his work, *e.g.*, in mills, breweries or stables. If desensitization with the particular allergen fails to produce benefit, a change of occupation must be advised.

**Specific Desensitization.**—Should the patient find it impossible to avoid the offending allergen, desensitization may be attempted. In the case of ingestants two methods are available. A solution of the offending article may be injected subcutaneously in increasing doses. Alternatively, minute quantities of the food itself may be added to the patient's diet and the amount gradually increased. Desensitization is much more frequently employed against inhalants. When sensitivity is multiple it is advisable to use a solution containing a mixture of the commoner inhalants, *e.g.*, feathers, dust, animal hair and orris root. A mixed inhalant solution, with full directions, may be obtained from C. L. Bencard, Gorgate Hall, Dereham, Norfolk. In general, it is advisable to start with the subcutaneous injection of 0.1 c.c. of the weakest solution and cautiously to increase this dose at intervals of from five to seven days according to the local reaction. The occurrence of a general reaction such as an asthmatic attack necessitates the reduction of the dose at the next injection. In order to minimize the risk of general reactions, 2 or 3 minims (0.12 to 0.17 c.c.) of adrenaline should be injected simultaneously. Specific desensitization is most successful where only one allergen is concerned. It has certain risks, fortunately rare, and should not be practised by those unfamiliar with the technique.

Before embarking on a course of desensitizing injections the patient should be told that the process involves frequent injections over many weeks. The idea that beneficial effects can be obtained from two or three injections is

fallacious. In our experience the benefits claimed to result from specific desensitization have been greatly exaggerated. Any improvement which may result is seldom lasting. We have already drawn attention to the great importance of the psychological factor in the treatment of asthma, which is particularly apparent when parenteral methods of treatment are employed by an enthusiast. Nevertheless, specific desensitization is believed to be of value by many authorities, and details of the technique have accordingly been given.

*Histamine.*—Evidence has been accumulating in favour of the view that many of the symptoms of allergic disorders are due to a release of histamine, and efforts have been made to desensitize the allergic patient to histamine by its injection in small doses. More recently a histamine azo-protein has been used for this purpose in the belief that histamine conjugated with a protein is more capable of stimulating histamine antibodies without producing typical histamine reactions. Lertigon (Parke, Davis) is a histamine azo-protein complex which has been used in the treatment of asthma with variable results. Antihistamine drugs—so valuable in the treatment of superficial allergies—are of little use in the treatment of asthma.

**Non-specific Desensitization.**—For this purpose many substances have been used, such as peptone, tuberculin, milk, T.A.B. vaccine, sulphur, etc. We do not intend to discuss these preparations in detail because we feel that their exponents have in general taken an unduly optimistic view of their value, and we suspect that the psychological effects of injections have been overlooked. While it is true that 60 to 70 per cent. of cases of asthma may obtain benefit by non-specific desensitization, in our experience the improvement is seldom lasting. Nevertheless, it is worthy of trial when other measures have failed. Occasionally, dramatic success is attained, while in other cases temporary relief occurs which enables the patient to regain his confidence.

*Peptone.*—Armour's peptone No. 2 (5 per cent. solution) is chiefly employed and can be given intravenously or intramuscularly, the latter route being considerably safer. Starting with 0.3 c.c. (5 minims), the dose is slowly increased every four or five days until a maximum of 2 to 3 c.c. is given, after which the dose is gradually reduced.

*Milk.*—Whole milk which has first been boiled may be injected subcutaneously or intramuscularly at intervals of five to seven days, starting with an initial dose of 1 c.c. and gradually increasing to a maximum dose of 10 c.c. The proprietary preparation "xifal milk" has been used for this purpose.

*Sulphur.*—Sulphur in colloidal form in 1 and 2 c.c. ampoules in 0.1 and 0.5 per cent. solution is marketed by British Drug Houses Ltd. and Crookes' Laboratories. It is given intramuscularly or intravenously at weekly intervals.

*T.A.B. Vaccine.*—The initial dose is 25 million organisms injected intravenously, which is increased by 25 to 50 million at weekly intervals up to a maximum of 500 million. The severe reactions which may occur necessitate great caution in this form of treatment.

*Autohæmotherapy.*—Five to ten cubic centimetres of blood are withdrawn into a syringe from a vein in the patient's arm and immediately injected into the muscles of the buttock. A course consists of six to ten injections at weekly intervals.

### THE INFECTIVE FACTOR

Acute infections of the upper respiratory tract will precipitate an attack of asthma in the majority of sufferers. Accordingly, the measures already described for the prevention and treatment of acute respiratory infections are particularly required in asthmatics (see p. 722 *et seq.*).

**Vaccines.**—Vaccines are recommended for the treatment of asthma: (1) if there is a history of asthma starting directly after severe respiratory infections; (2) if there is expectoration of a purulent sputum; (3) if there is evidence of lung damage as shown by clinical or radiological examination.

The question whether autogenous or stock vaccines should be employed, with details regarding dosage and technique, have been fully discussed on p. 724, and this information is equally relevant to the treatment of asthma. Many authorities believe that the vaccine treatment of asthma is extremely useful, but their investigations are seldom properly controlled. We believe that the anticatarrhal vaccines usually employed act in a non-specific rather than in a specific manner. Nevertheless, vaccine treatment is worthy of trial in cases of asthma with lung damage who have failed to respond to other forms of treatment. It is again necessary to recall that vaccines should be given cautiously and in amounts which fail to produce general reactions.

### THE NASAL FACTOR

A nasal factor is commonly present in asthma and is frequently of importance. There are two ways in which it may operate: (1) if the asthma-genic area in the nose is in an abnormally sensitive condition it will readily be irritated by dust, cold air, purulent material, etc., thus inducing through a reflex mechanism an asthmatic attack; and (2) organic diseases, such as polypi, deflected septum, hypertrophy of the turbinate bones and infections of the nasal sinuses, all tend to cause asthma, both by interfering with free ventilation and by increasing the liability to infections of the nose and throat.

In taking a careful history it is important to record the occurrence of sneezing, watering and itching of the nose prior to the asthmatic attack, whether the symptoms occur at any particular season of the year, and the effects, if any, produced on the patient by a dusty atmosphere. A positive history in these respects favours an allergic basis. Owing to the similarity of the symptoms of allergic rhinorrhœa and rhinorrhœa due to a vasomotor neurosis, skin tests may be required for their differentiation.

To determine whether organic disease is present an examination of the nose and throat should be made. A pale boggy colour of the mucous membrane of the nose suggests an allergic factor, while redness and congestion indicate infection. These appearances are deceptive where, as often happens, infection occurs in a mucous membrane already allergic. The presence of eosinophilia in the nasal secretion is a valuable indication of the importance of the allergic factor.

Experience has shown that the surgical treatment of nasal abnormalities in asthma is disappointing. It is true that relief is often obtained for a period of weeks or even months, but the majority of cases relapse. This suggests that many nasal abnormalities are not the cause of the asthma but its result. Accordingly, a conservative attitude should be adopted towards nasal surgery.

The asthma should be treated on the general lines indicated, while local measures should be employed to reduce the œdema and swelling of the mucous membrane of the nose. Freer ventilation will be secured along with better drainage of the accessory sinuses and lowered irritability of the asthmagenic area. This may be achieved by local application of the cautery, or of astringent and anæsthetic drugs, or zinc ionization (for details, see *Paroxysmal Rhinorrhœa*). Infected antra should be treated by proof puncture and lavage, rather than by open operation.

If the measures described fail to bring relief, the question of the correction of the nasal factor by surgical measures must be considered. The principle which we advocate is that radical surgical treatment should be advised only if the abnormalities present are such that even if the patient had not asthma, surgical measures would be necessary. The position should be explained to the patient without undue optimism.

### THE GASTRO INTESTINAL FACTOR

The gastro-intestinal factor may cause asthma either because the patient's digestion is upset by some article of food or for reflex reasons consequent on flatulent dyspepsia or constipation.

In general, it will be found that asthmatics do best if they take a good breakfast and lunch and a light evening meal. It is particularly important that they should take no food within an hour and a half of going to bed. While considerable latitude should be allowed the patient with regard to the composition of his diet, obviously he should avoid any food to which he is sensitive, and anything likely to cause dyspepsia and flatulence. Large meals should be prohibited, two or three courses being sufficient. Flatulent dyspepsia and constipation should be treated as outlined on pp. 552, 561.

In about one case in four an atonic dyspepsia accompanied by achlorhydria is present. In such cases benefit may be obtained from hydrochloric acid and pepsin (see p. 467). We are unwilling to accept the statement by several authors that the routine administration of hydrochloric acid or nitro-hydrochloric acid is of curative value in a high proportion of cases of asthma. Any benefit derived from giving 30 to 60 minims (1·74 to 3·48 c.c.) three times a day of hydrochloric acid to a patient whose stomach is already secreting hundreds of cubic centimetres of acid in the twenty-four hours can only be explained on psychological basis.

### DRUGS

**Sedative Drugs.**—Many asthmatic patients, particularly those in whom the psychological factor is prominent, live in a state of constant nervous tension. For such persons phenobarbitone in small doses of about  $\frac{1}{2}$  gr. (0·03 gm.) night and morning is of value.

**Antispasmodic Drugs.**—Chronic asthmatics, who have failed to respond to the various forms of treatment outlined above, should be instructed to inject themselves with adrenaline, the most useful drug available for the treatment of asthma. By this means many patients, who would otherwise be semi-invalids, can be enabled to live a practically normal life. A dose as small as 2 minims (0·12 c.c.), if given at the onset, may be sufficient to abort the attack. The patient should discover for himself the smallest effective dose. In

general, however, some degree of tolerance develops and it will be necessary, as time goes on, to increase the dose gradually. In addition, the knowledge that severe attacks may be prevented restores confidence, which so many asthmatics have lost. An injection of adrenaline in oil (see p. 755) given in the evening may procure freedom from bronchospasm during the night.

Although drug treatment is only palliative, the antispasmodic drugs are of value in the treatment of asthma. A mixture, if persistently used for several months, will often lessen the frequency and severity of the attacks. The drugs commonly employed are lobelia, stramonium or belladonna in the form of a tincture in doses of 10 to 15 minims (0.58 to 0.87 c.c.). The late Sir Arthur Hurst, a lifelong asthmatic himself, informed us that from personal experience he had found lobelia and belladonna of little value, but that stramonium in doses of at least 30 minims (1.74 c.c.) of the tincture, given at night for short periods, was worthy of trial. Unfortunately its effect in drying the pulmonary secretion and upsetting the digestion may outweigh any benefit derived from its antispasmodic action. Iodide of potassium is generally added to the mixture (see p. 773). Ephedrine sulphate and hydrochloride are valuable antispasmodics. While not so rapid or constant in its action as adrenaline, ephedrine has the advantages that it can be taken by mouth and has more lasting effects. The dose is  $\frac{1}{2}$  gr. (0.03 gm.) two or three times a day for an adult,  $\frac{1}{4}$  gr. (15 mg.) for a child over the age of seven,  $\frac{1}{8}$  gr. (7.5 mg.) for an infant.

Ephedrine may be added to the mixture of antispasmodic drugs described above, but we prefer to give it separately in tablet form so that it can be omitted from the evening dose should it lead to sleeplessness. Some persons are unable to take ephedrine because of the occurrence of unpleasant symptoms, such as nausea, palpitation, sweating and occasionally dysuria. These reactions may be prevented or at least reduced if ephedrine is prescribed with one of the following: phenobarbitone,  $\frac{1}{2}$  gr. (0.03 gm.); phenazone, 5 gr. (0.3 gm.); sodium amytal, 1 gr. (0.06 gm.).

Synthetic ephedrine (pseudo-ephedrine) is sold by leading manufacturing firms, *e.g.*, tabloid pseudo-ephedrine hydrochlor. (B. W. & Co.) and ephetonin (Napp). It is cheaper and produces unpleasant reactions less frequently than ephedrine. On the other hand, it is doubtful whether it is as efficacious as natural ephedrine in relieving bronchial spasm.

Theamin (Lilly), a theophylline compound, has recently been strongly recommended as a substitute for ephedrine. It is given in capsules containing  $1\frac{1}{2}$  and 3 gr. (0.09 and 0.18 gm.) two or three times daily, the former dose being suitable for children. Capsules containing amytal in addition to the Theamin are also available and are indicated when the nervous element in the case is predominant.

When asthma occurs principally at night a dose of a strong sedative linctus should be taken half an hour before going to bed. It may prevent the onset of coughing, which not infrequently occurs when the patient leaves the warm living-room and enters the cold bedroom. Antispasmodic drugs are included in the prescription. A single dose at night will often prevent the early morning bronchial spasm. The sedative drugs usually employed are tinct. opii camph. in doses of 30 minims (1.7 c.c.) or syr. codein phosphate, 1 drachm (3.6 c.c.) (see Appendix).

**Inhalations.**—Adrenaline, ephedrine and cocaine in oily and watery solutions may be used singly or in combination in the form of inhalations. The solution should be sprayed into the nose by means of a simple atomizer or by a pump worked by hand or driven by an electric motor or volatilized by oxygen. We recommend a hand atomizer, as it is equally efficient, more portable and much less expensive than the instruments worked by mechanical means. A high-grade atomizer should be used in order to deliver the finest possible spray. The original cost of the atomizer will soon be recovered by the less wasteful use of expensive drugs. Ephedrine 1 per cent. in 4 per cent. glucose saline with or without cocaine 1 per cent. will be found satisfactory. Ephedrine is preferable to adrenaline since its local effect is more prolonged and the secondary reaction less marked. Cocaine is an excellent astringent and local anæsthetic, while with a 1 per cent. solution there is practically no danger of habit formation.

Many patients prefer the inhalation to the injection of adrenaline, even though the effects are not so dramatic or prolonged. Moreover, the mere knowledge that they can readily avert an incipient attack of asthma gives considerable confidence and relieves anxiety and tension. Adrenaline hydrochloride in a 1 in 100 solution can be used for this purpose.

Inhalations of smoke from burning powders or cigarettes containing potassium nitrate with stramonium and lobelia leaves are commonly employed by asthmatics. In general they cannot be recommended because the temporary relief obtained is more than offset by the irritant effects on the bronchial mucous membrane.

**Other Drugs.**—Antihistamine drugs (see p. 96) have been advocated for the treatment of asthma, but in general the results have been extremely disappointing.

The use of morphia in the management of the asthmatic state is contra-indicated because of the dangers of habit formation and of pulmonary atelectasis.

The administration of glucose is useful in children, particularly if they are nervous or poorly nourished. It may be given in 1 or 2 teaspoonful doses after meals, or as honey or barley sugar.

Calcium has been employed in many forms in the treatment of asthma, but there can be no doubt that it is of little value.

Caffeine may be of value in all types of asthma, and particularly in elderly patients with some degree of cardiac weakness. Two to four tablets containing 3 gr. (0.18 gm.) of caffeine citrate may be taken before attempting an effort which tends to make the patient unduly breathless. Theamin (see p. 755) is claimed to be superior to caffeine in this respect. Caffeine should be avoided in the evening as it induces insomnia.

#### GENERAL MEASURES

Apart from the investigation and treatment of the special factors already described, the family doctor can always give valuable help by his common-sense advice on general health measures. Physical fatigue and nervous strain are potent factors in the production of asthma, and these must be counteracted by reorganization of the patient's life, both in regard to work and play. This entails careful investigation of the family, social and business relations of the patient, and, of course, each individual case must be treated on its own merits.



**Climate.**—Climatic conditions are believed to play an important part in asthma. In general, it may be said that a cool dry climate without marked variations in humidity and temperature is the most suitable. Many asthmatics feel much better when living in the mountains at an altitude of 3,000 ft. It has been suggested that high altitudes produce beneficial biochemical changes in the blood or that the pure air is free from allergens and mechanically irritating particles. Nevertheless, it is impossible to say what climate is suitable for each individual case of asthma. We have had patients who tell us that they keep free from attacks in Glasgow in spite of the fog and smoke, while others have come from Glasgow to Aberdeen to find relief in the cool, bracing air. This suggests to us that some at least of the benefits credited to a change of climate are in reality due to a psychological factor, since the climatic change is generally accompanied by the removal of disturbing influences which have kept the broncho-constrictor centre constantly irritated.

This aspect is well brought out by the following case history. Miss A. had to be removed from school in Aberdeen at the age of sixteen because of asthma. Her doctor ordered this on the grounds that the climate was the essential aetiological factor.

She went to her home in the country some forty miles away, where she remained free from asthma. At the age of eighteen she went to the University of Glasgow, where she was very happy, took part in many social activities and had no asthma. Having taken her degree, she returned home, and within six months asthma started again. She then took a post in Aberdeen as under-manageress of an hotel, and remained in this situation for three years, during which time she had only an occasional attack of mild asthma.

Our analysis of the psychological aspects of this case is as follows: While at school in Aberdeen she was unhappy and objected to the discipline. She reacted to this state of nervous tension by having asthma, which obtained for her sympathy and preferential treatment and finally enabled her to leave her unhappy surroundings. On returning to her home in the country, she was free from the restrictions which were imposed on her at school, and so she kept well. Her reaction to home life in the country was different on her return from Glasgow. The absence of cinemas, theatres and dances made existence in the country seem dull and monotonous, and home life now appeared to offer many restrictions compared to the freedom which she enjoyed in lodgings in Glasgow. Again she reacted to these psychological factors by having asthma. These in turn disappeared when she accepted a position in Aberdeen which gave her her freedom and satisfied her social desires. If our deductions are correct, climatic conditions had nothing to do with the onset or disappearance of the asthma, for it will be noted that at different periods of her life she had asthma and was also free from asthma in the same district.

**Spa Treatment.**—Enthusiastic spa physicians claim remarkable beneficial effects from the waters of their individual spas, whether administered internally, externally or by inhalation. Temporary beneficial effects are certainly frequent, but we have little hesitation in saying that they are largely due to the improvement in the patient's general health and mental outlook, which result from a holiday under pleasant conditions, and from the unintentional psychotherapy of the enthusiastic spa physician.

**Prevention of Upper Respiratory Infections.**—In the majority of sufferers the occurrence of any respiratory tract infection will precipitate an asthmatic attack. It is of the utmost importance, therefore, that every care should be exercised in their prophylaxis and treatment. Preventive measures have been fully described on p. 722.

**Postural and Breathing Exercises.**—Long-continued asthma leads to over-expansion of the lungs and changes in the thorax, which assumes the so-called barrel-shape with hypertrophy of the accessory muscles of respiration. In addition, the pulmonary distension leads to a state of emphysema, which, as Hurst has rightly pointed out, is for a long time functional rather than organic in origin. Lastly, the respiration of the chronic asthmatic becomes of the upper thoracic type through his failure to use the diaphragm and abdominal muscles. In consequence a considerable proportion of the air contained in the lower lobes becomes stagnant. For the treatment of these conditions postural and breathing exercises are of paramount importance. A large proportion of chronic asthmatics will derive marked benefit by undertaking a course of remedial exercises. This necessitates the help of a qualified physiotherapist, not only to give instruction in the physical exercises but to loosen the stiff thoracic muscles by applying massage. The book published by the Asthma Research Council, entitled "Physical Exercises for Asthma," fully describes suitable exercises in detail (obtainable for 1s. post free from the Secretary, King's College, Strand, London, W.C.2).

## HAY FEVER

Hay fever occurs in individuals who are hypersensitive to the pollen of grasses and is characterized by itching and watering of the eyes, sneezing and running at the nose, and a hacking cough.

The hay-fever season usually starts in the south of England about the middle of May and continues throughout June and July. In Scotland, the season is two or three weeks later. In America allergic symptoms to the pollen of ragweed are common in the autumn, usually from August to October.

**Symptomatic Treatment.**—When the grasses are pollinating the sufferer from hay fever should avoid country districts where the air is heavily laden with pollen, but pollen is so widely disseminated that severe symptoms may occur in the middle of a large city. In a severe case it may be necessary for the individual to remain indoors with the windows closed, only venturing out during damp and rainy weather. A long sea voyage may be recommended in the case of a wealthy patient. Special pollen filters can be purchased in the form of masks which the patient wears during the day. Such appliances, however, are cumbersome and seldom tolerated.

Conjunctivitis may be very distressing and painful. For its prevention and treatment close-fitting dark glasses should be worn. Immediate relief can be obtained by the instillation of 1 or 2 drops of the following solution into each eye:—

Liq. adrenal. hydrochlor.	1 : 1,000	.	.	fl. dr. 1 (3·6 c.c.)
Cocain. hydrochlor.	.	.	.	gr. 1½ (0·09 gm.)
Saturated solution boric acid	.	.	to	fl. oz. 1 (28·4 c.c.)

Ephedrine is an excellent substitute for adrenaline and may be instilled into the eye in a strength of 2 to 3 gr. (0.12 to 0.18 gm.) to the ounce (28.4 c.c.) of saturated boric solution.

The troublesome sneezing and irritation of the nose may be temporarily relieved by the instillation of nasal drops containing ephedrine in 1 to 3 per cent. solution in 4 per cent. glucose saline. A useful spray consists of 1 per cent. ephedrine sulphate and 1 per cent. cocaine in saline.

For the relief of the hacking cough a sedative linctus should be administered (see Appendix).

It is beneficial to prescribe ephedrine by mouth in doses of  $\frac{1}{2}$  gr. (0.03 gm.) night and morning. It may be combined with  $\frac{1}{2}$  gr. (0.03 gm.) phenobarbitone or  $\frac{3}{4}$  gr. (0.04 gm.) sodium amytal if any untoward effects are experienced.

Since many sufferers from hay fever are nervous individuals, it is well to prescribe small doses of a mild sedative throughout the season.

Antihistamine drugs (see p. 96) often afford striking symptomatic relief to sufferers from pollen allergy and are always worth a trial.

**Pre-seasonal Specific Desensitization.**—Pre-seasonal specific desensitization entails the subcutaneous injection of pollen extract in increasing quantities before the onset of the hay fever season. Suitable extracts may be obtained from leading manufacturing firms (Parke, Davis & Co., Bencard, Duncan & Flockhart, etc.). The solution is supplied in rubber-capped bottles containing so many units of pollen per cubic centimetre. The results of pre-seasonal desensitization have varied in the hands of different writers, but it may be said that the practitioner can expect complete relief or marked improvement in the majority of cases. A very small number may be completely cured by one course of injections, but the majority of patients will require desensitization during successive years. After a number of courses, many patients will be able to enjoy considerable comfort for the next year or two. The majority, however, return to their former condition, requiring further desensitization.

Treatment must be commenced at least ten weeks before the beginning of the pollen season, *i.e.*, about the end of February or in the first week of March.

Intradermal skin tests should first be carried out to determine the degree of sensitivity. Very sensitive cases may not tolerate more than five units of pollen extract for an initial dose, while the least sensitive cases can receive 500 units. The extract is given subcutaneously at intervals of four to seven days, and the dose should be gradually increased until a maximum of 100,000 units is reached before the onset of the hay-fever season. This dose should be repeated weekly for three to four weeks after the season commences. After the needle of the syringe has been inserted it is important to withdraw the piston to ensure that the point of the needle is not in a small vein. The intravenous injection of pollen extract may give rise to a severe general reaction. To each injection, 2 minims (0.12 c.c.) of adrenaline (1:1,000 solution) should be added in order to slow the rate of absorption and lessen the risk of a general reaction. After the injection the patient must be kept under observation for half an hour in case any local or general reaction occurs.

*General Reactions* are fortunately rare, but may be alarming and even fatal. Prompt measures must be adopted as soon as the first symptoms

appear. Itching of the palms of the hands and conjunctivæ are indications that a general reaction is commencing. An immediate injection of  $\frac{1}{2}$  c.c. of adrenaline should be given subcutaneously. To prevent further quantities of pollen extract reaching the circulation a tourniquet should be applied to the arm proximal to the site of injection. If more severe symptoms such as urticaria, swelling of the neck and face, asthma or collapse occur, a further injection of 1 c.c. of adrenaline must be given. If the patient is in a state of collapse artificial respiration must be started at once and 2 c.c. of nikethamide injected intramuscularly. The occurrence of a general reaction calls for a reduction of the next dose of extract to one quarter and this should be combined with 5 minims (0.3 c.c.) of adrenaline. Subsequent doses must be increased cautiously.

*Local Reactions* are more frequent and are evidenced by redness, swelling and itching at the site of injection. The schedule of dosage need not be interrupted for a mild local reaction, but if it is large and painful the subsequent injection should be repeated instead of being increased.

Desensitization by "rush inoculation" as advocated by Freeman may be used if sufficient time is not available for the full pre-seasonal course of injections. This method is not without danger and should only be practised by those with experience in the treatment of allergy. The course, which consists of subcutaneous injections of pollen extract every one and a half to two hours, may be completed in from two to four days.

**Perennial Desensitization.**—The perennial method has given good results in some hands and poor results in others. Monthly injections are given throughout the year, the dose being the highest dose attained at the end of the first pre-seasonal course. This method obviates the necessity of frequent visits to the practitioner.

**Seasonal Desensitization.**—Desensitization may still be attempted even when the patient presents himself after the symptoms of hay fever have appeared. The initial dose is calculated from the degree of the patient's sensitivity to pollen extract as determined by intradermal skin tests. It varies from 5 to 500 units and is given daily for three to five days. The dose is then increased cautiously and the intervals between injections lengthened. The danger of serious reactions and the uncertainty of success obtained make it doubtful if desensitization should be attempted when the patient is actually suffering from hay fever.

**Zinc Ionization.**—Zinc ionization as employed for the treatment of paroxysmal rhinorrhœa has given good results in hay fever. It should be carried out at the commencement of the hay-fever season and in most cases will have to be repeated on two or three occasions during the season.

**Conclusions.**—Pre-seasonal specific desensitization is advised as the method of choice if antihistamine drugs do not control the symptoms.

Desensitization by the oral route or by the local application of pollen ointment cannot be recommended because of the disappointing results obtained.

Seasonal desensitization should not be undertaken by the general practitioner because of the dangers involved. If the patient presents himself for treatment while suffering from hay fever, reliance should be placed on symptomatic treatment.

## PAROXYSMAL RHINORRHOEA

(*Vasomotor Rhinitis*)

Paroxysmal rhinorrhœa is a condition characterized by paroxysms of sneezing and watery discharge from the nose. In many cases it is allergic in nature, being often found in association with asthma. The allergens responsible are usually inhalants such as pollens, horse dander, dust, orris root and flour. Foods (wheat, egg, fish) are rare causes, and drugs, especially aspirin, are occasionally responsible for allergic nasal symptoms.

Sensitivity to one or more allergens may be revealed by a detailed history combined with intradermal skin tests (see p. 770), which should always be performed. In many cases, however, no evidence of allergy can be found. In these a hypersensitivity to bacterial proteins may be present, or more frequently a state of "primary vasomotor disturbance" is present for which no satisfactory explanation may be available.

The first step is to exclude from the patient's environment all allergens to which he shows hypersensitiveness (see p. 769). If this is impossible, or if the condition does not improve, specific desensitization should be carried out. This entails weekly subcutaneous injections of extracts of the offending allergen or allergens in increasing concentration. It is usual to start treatment with a weak extract, the initial dose of which is 0.1 c.c. The solutions may be obtained from Messrs Bencard.

The general health should be maintained by the usual measures and care should be taken to avoid fatigue, worry and cold, which are important precipitating factors. Varnish, smoke and perfumes often act as mechanical irritants and are liable to produce an attack. If the patient's work entails spending many hours in a dust-laden atmosphere, a change of occupation may be desirable.

Striking relief may be obtained during a paroxysm by the application of astringent drugs to the nasal mucous membrane. Ephedrine is extensively used and may be applied to the nose as an ointment, 5 gr. (0.3 gm.) to 1 oz. (31.1 gm.) of soft paraffin, alone or with adrenaline 1 gr. (0.06 gm.) to 1 oz. (28.4 c.c.). Probably better results are obtained by the use of an oily or aqueous solution containing 0.5 to 1 per cent. of ephedrine. Nebula ephedrinæ co. or "endrine" may be dropped into the nose or may be used in an atomizer. If the preparation is being used over a long period, the use of an atomizer is much more economical. Amphetamine which is supplied in inhalers is also useful. These preparations should not be used more than four or five times a day. Ephedrine by mouth in doses of  $\frac{1}{2}$  gr. (0.03 gm.) night and morning is also helpful in preventing and relieving attacks.

Treatment with antihistamine drugs (see p. 96) is helpful in a proportion of cases, though the results are not as strikingly good as in hay fever.

Zinc ionization of the nose is widely used, but results seem to show that it is most successful in cases in which no specific allergen can be found. The treatment involves packing the nasal cavities with gauze soaked in 2 per cent. zinc sulphate solution through which an electric current is passed.

Many cases can be relieved temporarily by cauterization to the inferior turbinates, using either a saturated solution of trichloroacetic acid or chromic acid (40 per cent.) or a fused bead of silver nitrate. The electro-cautery,

heated to a cherry-red heat, is also effective and may be applied to Francis' area or tubercle of the septum.

It is generally agreed that no operation, however trivial, should be undertaken until the allergic symptoms have subsided or have been brought under control. Operative procedures on the nose and throat frequently fail to cure paroxysmal rhinorrhœa. Accordingly, surgical treatment is contraindicated except for the correction of pathological conditions irrespective of the presence of paroxysmal rhinorrhœa. The aim of surgical treatment should be restoration of function and the elimination of infection. Infected adenoids and tonsils, sinusitis, polypi and deflected septum, should be treated on the usual lines.

# APPENDIX

## NASAL OR THROAT SPRAYS

Ephed. Hydrochlor.	.	.	.	1 per cent.
Glucose	.	.	.	4 per cent.
Normal Saline	.	.	to	fl. oz. 1 (28.4 c.c.)

Nebula ephedrinæ co., B.P.C.

Contains approximately—

Ephed. Hydrochlor.	.	.	gr. iv (0.24 gm.)
Menthol.	.	.	gr. ix (0.54 gm.)
Camph.	.	.	gr. ix (0.54 gm.)
Oil of Thyme	.	.	℥x (0.58 c.c.)
Paraff. Liq.	.	to	fl. oz. 1 (28.4 c.c.)

Nebula eucalyptol co., B.P.C.

Contains approximately—

Eucalyp.	.	.	℥xl (2.32 c.c.)
Camph.	.	.	gr. ix (0.54 gm.)
Menthol.	.	.	gr. ix (0.54 gm.)
Thymol.	.	.	gr. ½ (0.03 gm.)
Paraff. Liq.	.	to	fl. oz. 1 (28.4 c.c.)

## ANTISPASMODIC COUGH MIXTURE

R	Pot. Iod.	.	.	gr. v (0.3 gm.)
	Tinct. Bellad.	.	.	℥x (0.58 c.c.)
	Tinct. Stramon.	.	.	℥xv-xx (0.87-1.16 c.c.)
	Ext. Glycyrrh. Liq.	.	.	℥xv (0.87 c.c.)
	Aq.	.	ad	fl. oz. ½ (14.2 c.c.)

## SEDATIVE ANTISPASMODIC MIXTURE

R	Ephed. Hydrochlor.	.	.	gr. ½ (0.03 gm.)
	Tinct. Stramon.	.	.	℥xv (0.87 c.c.)
	Syr. Codein. Phos.	.	ad	fl. dr. 1 (3.6 c.c.)

## EXPECTORANT COUGH MIXTURES

R Ammon. Carb. . . . . gr. v (0.3 gm.)  
 Pot. Iod. . . . . gr. iii (0.18 gm.)  
 Tinct. Ipecac. . . . . ℥<sub>x</sub> (0.58 c.c.)  
 Ext. Glycyrrh. Liq. . . . . ℥<sub>xv</sub> (0.87 c.c.)  
 Aq. . . . . ad fl. oz.  $\frac{1}{2}$  (14.2 c.c.)

R Ammon. Chlorid. . . . . gr. x (0.6 gm.)  
 Tinct. Scill. . . . . ℥<sub>x</sub> (0.58 c.c.)  
 Sp. Chlorof. . . . . ℥<sub>x</sub> (0.58 c.c.)  
 Syr. Tolu. . . . . ℥<sub>xxx</sub> (1.74 c.c.)  
 Aq. . . . . ad fl. oz.  $\frac{1}{2}$  (14.2 c.c.)

## ALKALINE COUGH MIXTURE

R Sod. Bicarb. . . . . gr. xx (1.2 gm.)  
 Pot. Citrat. . . . . gr. xxx (1.8 gm.)  
 Liq. Ammon. Acet. Dil. . . . . fl. dr. ii-iv (7.2-14.4 c.c.)  
 Aq. Chlorof. . . . . ad fl. oz.  $\frac{1}{2}$  (14.2 c.c.)

## SEDATIVE LINCTUSES

## 1. Linctus scillæ co., B.P.C.

Contains—

Tinct. Opii Camph.	.	.	.	.	.	} Equal parts
Oxymel scill.	.	.	.	.	.	
Syr. Tolu.	.	.	.	.	.	

Dose— $\frac{1}{2}$  to 1 fluid drachm (1.8 to 3.6 c.c.)

## 2. Linctus diamorphin. et scillæ, B.P.C.

Contains—

Diamorphine hydrochloride . . . gr.  $\frac{1}{10}$  in each fluid drachm  
 (1.5 mg. in each 3.6 c.c.)

Dose— $\frac{1}{2}$  to 1 fluid drachm (1.8 to 3.6 c.c.)

## 3. Syr. Codein. Phosph., B.P.C.

Contains—

Codein. Phosph. . . . . gr.  $\frac{1}{4}$  in each fluid drachm  
 (15 mg. in each 3.6 c.c.)

Dose— $\frac{1}{2}$  to 2 fluid drachms (1.8 to 7.2 c.c.)

## 4. Elixir diamorphin. et terpin., B.P.C.

Contains—

Diamorphine hydrochloride . . . gr.  $\frac{1}{8}$  in each fluid drachm  
 (3.3 mg. in each 3.6 c.c.)

L. S. P. DAVIDSON.  
 I. GORDON.

# RENAL DISEASES

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## NEPHRITIS

### INTRODUCTION

**A**LTHOUGH the classification of nephritis has been obscured by the over-elaboration and subdivision of most workers, the treatment fortunately remains fairly clear. That this is so is mainly due to the fact that its basis rests upon no pathological classification but is almost wholly symptomatic, being regulated by the nature and the degree of the renal upset. It is therefore necessary to preface the treatment of nephritis with a short discussion of the changes which are present in the kidney at the various stages of the disease. The acute stage develops in most cases seven to twenty-one days after a streptococcal condition in some other part of the body, most commonly the throat. This may have been so slight as to have been forgotten or never noticed by the patient. With the onset of nephritis the glomeruli are rendered ischæmic for a brief period, which is yet sufficiently long to cause damage to the glomerular membrane and the tubule. As a result the permeability of the glomerular membrane is increased while the concentrating power of the tubule is diminished. Consequent upon the glomerular ischæmia and its sequelæ are the characteristic findings of acute nephritis, namely, oliguria, blood, albumin and tube casts (blood and epithelial) in the urine, impairment of concentrating power, increase in the nitrogenous constituents of the blood, raised blood pressure and œdema. As initial improvement occurs, blood diminishes in the urine, while the output increases; œdema diminishes; blood pressure falls and nitrogen retention disappears. Later the œdema disappears while the albuminuria diminishes and still later, in most cases, clears up entirely. The concentrating power of the kidney, however, takes longer to be restored. In most cases the restoration of normal concentrating power is the final proof of recovery. The treatment of acute nephritis is determined by the stage present as detailed above.

Complete recovery occurs in the majority of cases where treatment is patiently persevered with. Failing this complete recovery, the condition may pass on to the second stage of glomerulonephritis characterized by the persistence of increased glomerular permeability but little or no impairment of the concentrating power of the tubule. At this stage, therefore, albuminuria is the predominant sign, being present for long periods without associated œdema, which, however, develops eventually in most cases. The characteristic blood chemistry findings are a lowered plasma albumin content and an increased concentration of cholesterol. There is no nitrogenous retention, impairment of renal function nor hypertension with its associated cardiac changes.

The third stage of glomerulonephritis is marked by sclerosis of the affected glomeruli and, consequent upon the withdrawal of blood from these, the albuminuria disappears. Because of the reduction in the number of



functioning kidney units, impaired concentrating power associated with the occurrence of azotæmia develops. Chemical analysis of the blood shows an increased nitrogenous content, and later there may be found decreased calcium and increased phosphorus contents and lowered  $\text{CO}_2$  combining power. Hypertension with its associated cardiovascular and retinal changes is also present.

It has to be understood that the above simple clear-cut division into the three stages of nephritis is seldom encountered clinically. Gradations from the one stage to the other are commonly found, so that treatment may have to be adapted to meet the requirements of patients who have signs and symptoms of two stages of the disease.

True uræmia, regarded as a symptom complex due to retention in the blood of urinary waste products consequent upon defective renal function, occurs in the third stage of glomerulonephritis. In the first stage of glomerulonephritis headache, amaurosis, convulsions and other focal symptoms and unconsciousness result from hypertensive encephalopathy and are not due to true uræmia. As the causation and symptomatology of the two conditions vary, so does the treatment.

### FIRST STAGE OF GLOMERULONEPHRITIS

#### *(Acute Nephritis)*

Treatment is based upon a consideration of the characteristics of the typical case and the normal course followed towards recovery. At the onset of the condition the aim should be to avoid irritation of the damaged organ and to give it functional rest, imposing upon it no avoidable strain until complete recovery has been obtained. The treatment therefore must run parallel with the functional ability of the kidney. Due regard must, however, be paid to the general condition of the patient, this being maintained at the highest possible level so that the desired renal recovery may be facilitated.

**Rest.**—Rest in bed is essential from the moment of diagnosis. It has been customary to place the patient in blankets and clothe him in flannel, but, now that sweating is not resorted to in treatment, these procedures may be modified provided the patient is always kept warm and free from draughts. The duration of rest in bed should be much longer than has been generally advised. Too often the disappearance of albuminuria is regarded as the index of cure; impairment of concentrating power is present in the majority of cases long after the urine is free of albumin; no patient should be allowed out of bed until complete recovery has taken place, *i.e.*, until the urine, blood pressure and blood chemistry are normal and the concentrating power has been fully restored. This may even entail complete rest in bed for months. As long as there are indications of improvement this treatment should be continued; when the condition becomes stationary, the advisability of allowing the patient up has to be admitted and future treatment must follow along the lines indicated later for the chronic

**Diet.**—*Protein and Fluid.*—The dietetic treatment most generally followed at the onset of the condition is the complete elimination of all protein—glucose and fruit juices being the sole sources of food. The fluid intake is restricted until the signs of acute damage are waning. For this

purpose  $1\frac{1}{2}$  to 2 pints of fluid only are permitted until the hæmaturia has diminished and diuresis has occurred. Volhard goes even further and advises complete withdrawal of fluid and food. Supporters of this line of treatment suggest that they are thereby lessening the burden on the kidney by providing it with no extra water and no exogenous nitrogen for excretion. It has to be borne in mind, however, that endogenous nitrogen is constantly being produced from tissue breakdown and consequently, even on a protein-free diet, a certain amount has to be excreted by the kidney or retained in the blood. Further, tissue breakdown without tissue replacement means deterioration of the general condition and decreased resistance to infection. Formerly milk was permitted in the acute stage, the diet consisting of milk in amounts up to 3 pints per day. Such a diet contains 1,680 c.c. of water, 60 gm. of protein and 3 gm. of sodium chloride. Admittedly this amount of protein is in excess of the requirements for the tissue needs of a resting individual. It has to be remembered that in caseinogen all the essential amino acids except cystine are present and that this is found in lactalbumin. Further, with a strictly limited administration of essential protein the nitrogen excretion is no greater than when protein has been wholly withheld. Up to 20 oz. of milk can be given without increasing the daily excretion of urea. It has accordingly been the writer's custom to compromise between these two methods in the treatment of the initial stage, giving alternate two-hourly feeds of citrated milk and glucose fruit-juice solution, the total amount of fluid over twenty-four hours being restricted to not more than 2 pints (see p. 784, Diet I). The protein in this quantity of milk has been shown to cause no rise above the endogenous level in the nitrogenous content of the urine of a normal individual, and is not likely to do so in any but the severest cases of acute nephritis characterized by almost complete anuria. The citrate assists the kidney to secrete a more bland, neutral or mildly alkaline urine. Following the appearance of diuresis and the lessening of the hæmaturia, the caloric intake is increased by the addition of further carbohydrates and fat, as bread, cereals, fruit, butter and cream. By this means the dietetic intake is raised to 1,500 calories per day, and this is continued until the hæmaturia has disappeared. At this stage it is advisable to carry out a renal function test to determine the concentrating power of the kidney because this gives a guide as to the protein intake to be allowed. The writer is in the habit of employing Calvert's urea concentration range, details of which are given below.<sup>1</sup> For those unable to carry out a urea concentration test, valuable information can be obtained from estimating the specific gravity of the first specimen of urine passed in the morning, provided a heavy albuminuria is not present. The specific gravity of this specimen in a normal individual should be 1,020 to 1,025; the lower the specific gravity, the less the protein that can be given with safety. As the patient on Diet I (see p. 784) is not in nitrogen balance, the daily protein

<sup>1</sup> *Urea Concentration Range.*—Fluid intake is restricted from noon. At 10 P.M. patient is given 15 gm. urea in 100 c.c. of water flavoured with orange. Bladder is emptied at 11 P.M. and urine discarded. Any urine passed before 7 A.M. is kept (specimen 1) and bladder emptied at 7 A.M. (specimen 2). Two pints of fluid are given at 7 A.M.; urine voided and discarded at 8 A.M.; and bladder emptied and specimen 3 kept at 9 A.M. Specimen 1 or 2 contains the maximum urea concentration and specimen 3 the minimum concentration.

A normal kidney shows a maximum power of 3.5 per cent. or over and a minimum of 0.4 per cent. or less. Early inefficiency is shown by fall in the maximum. As inefficiency advances, the maximum continues to fall while the minimum rises. In extreme inefficiency the maximum and minimum approximate (maximum under 1.5 per cent., minimum up to or over 1 per cent.).

intake must be increased to 50 gm. within a fortnight. Care must be taken that the additional protein is of high biological value (*i.e.*, protein of meat, fish, milk, cheese or eggs). Thereafter a renal function test is reapplied at regular intervals, and as the concentrating power of the kidney improves or the specific gravity of the urine increases the protein content of the diet is raised. When a maximum concentration of up to 2.5 per cent., or specific gravity of 1.018, is reached, a protein intake of 75 gm. may be given: a rise in the maximum to 3 per cent. or over (specific gravity, 1.020+) permits the giving of a normal diet with 90 gm. or over. A suitable dietetic scheme of treatment throughout all phases of this condition is given in Diets I to IV (pp. 784-785). The presence of albuminuria is not regarded as an indication for altering these dietetic measures. The above protein intakes are within the limits of the kidney's ability to deal with urea; the allowance of this full amount of protein ensures the maximum restoration of the general condition which deteriorates with too low protein intakes. Further, the writer wishes to emphasize the need for allowing the maximum protein intake consistent with the renal power present at any particular phase. It is now becoming increasingly accepted that such a procedure stimulates the return of kidney function and gives an earlier restoration of power than the previously adopted course which aimed at sparing the kidney.

**Salt.**—The part played by sodium chloride in the occurrence of oedema is still debated, but it would appear that of the two ions sodium is the more important. It is necessary, therefore, to limit the intake of sodium, but the food need not be made unpalatable by the withdrawal of chloride which can be administered in sufficient amount for savouring purposes by the use of potassium chloride.

**Vitamins.**—The vitamin content of the diet should be maintained throughout in view of the influence of these factors on infective processes (vitamins A and D) and capillary permeability (vitamin C). Vitamins A and D can be given as liq. vitamin A et D conc. Sufficient vitamin C should be provided in fresh juice of citrus fruits, vegetables and milk.

**Focal Sepsis.**—In the majority of cases the streptococcal infection preceding the acute nephritis requires no treatment by the time the kidney is affected. Unfortunately no certain prophylaxis can be adopted to prevent nephritis following such an infection. Nevertheless it may be that the lesion is present along with the nephritis, and sulphanilamide may be used in full doses without detriment to the renal state, owing to its high degree of solubility (see p. 81). Penicillin has also been employed with success at this time.

Continuing sepsis retards the recovery of many cases and a thorough search for foci of sepsis should always be carried out when progress appears to be slow. Teeth, tonsils and sinuses call for special attention. The surgical removal of the focus should not be postponed if hæmaturia and oedema persist or natural diuresis is delayed. Penicillin should be given in doses of 20,000 to 40,000 units three-hourly for three days before, and a further three days after, the operation. With the aid of such prophylactic treatment any focus of sepsis can be dealt with without exacerbating the renal condition.

**Drugs.**—**Alkalis.**—The administration of drugs is of little service in the treatment of acute nephritis. Alkalis are of value in rendering the urine more bland, and for this purpose potassium citrate and potassium bicarbon-

ate should be given in sufficient doses to keep the urine alkaline to litmus. Twenty to thirty grains (1.2 to 1.8 gm.) of each at four-hourly intervals may be required initially, but later this dose can be decreased. Alkalis can be administered conveniently along with the milk.

*Diuretics.*—Potassium citrate is the only diuretic that is permissible. The purine group (caffeine, theobromine and theophylline) act as kidney irritants; urea may already be present in the blood above the normal amount; the mercurial preparations, though excellent in cardiac failure even in the presence of albuminuria, are strongly contraindicated in acute nephritis. As the acute state passes off, diuresis will occur naturally. It cannot be urged too strongly that this natural diuresis be awaited patiently.

*Purgatives.*—The use of massive doses of jalap, salts and other drastic cathartics is fortunately now generally discontinued. The improvement (if any) which followed the fluid removal which they achieved was heavily outbalanced by the strain which they occasioned the patient. An easy motion once daily, achieved, if need be, by the aid of a mild aperient (cascara, senna, etc.), is all that is necessary. Mercurial purgatives are contraindicated on account of their possible irritant action on the kidney.

*Diaphoretics.*—Diaphoretic measures are now generally abandoned. Except, possibly, in incipient "acute uræmia" the drastic sweating by hot packs, hot baths and pilocarpine cannot be recommended. Even in incipient "uræmia" its value lies in the elimination of water, not of nitrogenous products as previously stated, and the withdrawal of water from the tissues can be more efficiently and easily secured by the means detailed below.

**Symptomatic Treatment.**—The measures discussed above are sufficient in the vast majority of cases, but in a few the appearance of certain special symptoms and signs calls for further treatment. Of these anuria, excessive oedema and "acute uræmia" are the chief.

*Anuria.*—Oliguria naturally relieved by diuresis in the course of a few days occasions no alarm or need for treatment other than the above; complete suppression necessitates an attempt to force kidney action. The most suitable method is the intravenous drip administration of 500 c.c. of a solution of 4.285 per cent. sodium sulphate and 10 per cent. glucose in normal (0.9 per cent.) saline. Where signs of tetany are present 5 to 10 c.c. of calcium gluconate (5 or 10 per cent.) may be given intramuscularly.

*Edema.*—Edema seldom fails to yield to the dietetic and general measures detailed above. In a few cases, however, persistent excessive oedema, ascites and hydrothorax are encountered and these must be treated by mechanical means. (For technique, see pp. 944, 945.) The impaired renal function contraindicates the high protein diet and urea administration recommended for removal of oedema in chronic glomerulonephritis (second stage). The necessity for the avoidance of drastic diuretics and the inefficacy of cathartic and diaphoretic measures have already been sufficiently stressed.

*Hypertensive Encephalopathy.*—The "uræmia" encountered in acute nephritis is due to oedema of the brain rather than to true uræmia, the resulting symptoms of hypertensive encephalopathy being all due to increased intracranial tension, possibly associated with high blood pressure. The gastro-intestinal symptoms found in true uræmia are usually absent. Venesection, with removal of 10 to 20 oz. of blood according to age and general condition, and lumbar puncture removing 30 to 40 c.c. of cerebro-

spinal fluid, may yield dramatic results. After lumbar puncture care must be taken to keep the head low lest a pressure cone develop. The administration of hypertonic solutions can be strongly recommended; rectally 8 oz. of 25 per cent. magnesium sulphate; intramuscularly 6 to 10 c.c. 25 per cent. magnesium sulphate; and intravenously 10 to 20 c.c. 10 per cent. magnesium sulphate, or 40 c.c. 30 per cent. sodium chloride, or 200 c.c. 50 per cent. glucose, or 50 per cent. sucrose are all measures which may be adopted to lower the intracranial tension. If intravenous administration is employed, a preceding venesection will add to the value of the therapy. Of the above alternative procedures the intravenous administration of hypertonic glucose or sucrose is the most successful. If acidosis is present, hypertonic solutions of glucose and sucrose fail to produce diuresis, so that they should then be given with alkalis.

After complete recovery from acute nephritis no dietetic restrictions are necessary. This point requires stressing as too frequently restriction of protein is unnecessarily imposed. The patient should, however, be warned about the danger of exposure to chills and wettings. He should be advised to treat all future infections, particularly those of the throat region, with special care. Instruction should be given in regard to the wearing of warm clothing and thick footwear in winter weather and to the need for changing the shoes and socks if they are wet.

## SECOND STAGE OF GLOMERULONEPHRITIS AND NEPHROSIS

*(Chronic Parenchymatous Nephritis, Nephrotic Syndrome, Hydræmic Syndrome, Chronic Nephritis with Œdema, Hydropigenous Nephritis, Type 2 Nephritis)*

It is customary to regard this stage as being characterized by the presence of a heavy albuminuria, but by the absence of azotæmic and hypertensive changes. The drain upon the plasma albumin by the heavy albuminuria results in a lowering of the protein osmotic tension of the blood. An important factor, secondary to this hypoproteinæmia and resultant œdema, is the passage in excess of sodium from blood to tissues. The absence of azotæmia is associated with a normal renal efficiency as demonstrated by renal function tests.

In *chronic nephrosis* a very similar clinical picture is present. There is heavy albuminuria, œdema and a normal renal concentrating power. The changes in blood chemistry are characterized by lowered plasma albumin, markedly increased cholesterol and a normal nitrogen content.

It is not fully realized that for long periods a patient may remain œdema-free despite constant albuminuria and that it is not until the plasma albumin concentration falls below 3 gm. per cent. (normal albumin being 4 to 6 gm. per cent.) that œdema occurs. Further, it has to be remembered that the general condition has to be maintained at all costs as patients with this disease show a greatly increased tendency to septic diseases. In the treatment of this condition one should concentrate on raising the lowered plasma albumin content and on improving the general condition of the patient, largely ignoring the albuminuria which is usually a permanent feature. For this purpose a high protein diet is necessary: 150 gm. per day or even more may be given if the patient can take it. With such a protein intake ample potential replenishment of plasma albumin is made and the urinary loss thereby compensated for, while at the same time the general condition of

the patient is maintained. At this stage of the disease the kidney has no difficulty in eliminating the end products of protein metabolism, hence no objection can be taken to such a régime on the basis of the increased urea production which it entails. Indeed, the increased urea excretion aids in eliminating œdema by promoting diuresis. Further, as there is no hypertension, the possible pressor action of protein need not be considered. A suitable high protein diet is given in Diet V (p. 786).

The salt intake should be limited, especially when the plasma albumin is falling towards the level at which œdema occurs. A safe rule at all times is to allow no salt to be added at table. Unless œdema is present, however, no objection may be taken to its moderate use in cooking. The rôles of the Na and Cl ions have been discussed under acute nephritis. Many of the nephritic diets are barely adequate in iron for the increased needs of the nephritic patient and consequently iron in any of the usual forms may be necessary (see p. 470). The vitamin content is also commonly deficient and should be supplemented. Septic foci must be searched for and, if present, eradicated. When œdema is present the daily fluid intake should not exceed 2 pints. When the patient is free of œdema it is unnecessary to restrict the fluid intake, this being guided by the patient's own desire. If the fluid intake is unduly restricted, it adds to the kidney's difficulty in excreting the large amount of nitrogenous waste products resulting from the high protein intake. On the other hand, it is unnecessary to force fluids upon the patient at this stage of the disease.

As long as œdema is absent the patient should be allowed to be up and to perform his usual occupations. He must, however, be guarded against chills and intercurrent infections which are likely to accelerate his downhill progress. When œdema develops he must be put to bed and a more drastic régime instituted, including a high protein salt-poor diet. In addition, diuretic measures have to be considered. Attempts to raise the osmotic tension of the plasma by the intravenous administration of 15 to 30 per cent. solution of acacia (1 gm. of acacia per kilogram body-weight) are reported to have been helpful, but in the writer's experience this procedure has not proved efficacious. The intravenous administration of plasma or protein hydrolysates, although theoretically logical, is found in practice to lead to no more than temporary improvement and has no material effect on the patient's progress. Osman recommends massive doses of alkali, giving sufficient citrate and bicarbonate to maintain the pH of the urine constantly at or above 8. Again, the writer has not found this method of treatment helpful. The administration of diuretics also holds out little hope of success. Diuretics are unlikely to be successful unless the hypoproteinæmia is corrected. Of the diuretics, urea may be given in doses of 100 to 250 gr. (6.5 to 16 gm.) t.i.d., this amount being easily excreted by the normally functioning kidney in addition to that produced from the high protein intake. The use of the mercurial diuretics is not without danger, especially if there are signs of acute renal damage. It is advisable to start with a small test dose of  $\frac{1}{2}$  c.c. only of mersalyl, and this should be given intramuscularly and not intravenously. (See treatment of cardiac œdema, p. 647.) Premedication with ammonium chloride or other acid salt can be given, as at this stage of chronic nephritis acidosis and uræmia do not occur.

Frequently, the removal of fluid by mechanical means is followed by rapid improvement. Paracentesis abdominis and thoracis are commonly

followed by diuresis and lessening of the œdema. Subcutaneous tapping is less often successful. The technique of these procedures is given on pp. 944, 945. The inadvisability of drastic purgation and diaphoresis has already been noted (p. 779).

Epstein recommends thyroid administration in the treatment of nephrosis. It has been noted that patients with nephrosis frequently tolerate large doses of thyroid. The writer has not found this of much value. Nor does the administration of suprarenal cortical extract in large doses intravenously prove any more successful. This latter attempt at endocrine therapy is based upon the supposed controlling influence of the suprarenal cortex upon cholesterol metabolism which is presumably grossly disturbed in nephrosis.

### THIRD STAGE OF GLOMERULONEPHRITIS

#### *(Chronic Interstitial Nephritis, Azotæmic Nephritis)*

When the condition reaches this stage, the affected glomeruli become sclerosed, blood flow through them is thereby prevented, and consequently albuminuria and œdema diminish or disappear. The reduction in nephrons, however, leads to impairment of concentrating power and other renal functions. This eventually gives rise to the characteristic changes in the blood chemistry of which the increased nitrogen content is the most frequently noted. At the same time hypertension develops with associated cardiac and retinal changes.

In the stage of azotæmia the diet can no longer be maintained at a high protein level but has to be based upon the power of the kidney to excrete nitrogenous waste products. Too often in the past, however, protein intake has been drastically curtailed with resultant damage to the general health. *It may safely be said that more damage can be done at this stage by protein starvation than by protein excess.* The degree of renal function should be determined by renal efficiency tests and by estimation of the blood nitrogen. These estimations should be repeated at intervals to ascertain the progress of the condition, the diet being regulated by the result. The diets given in Diets II to IV under Acute Nephritis can again be employed, starting with Diet IV (p. 785), where only a mild degree of functional impairment is present, and then descending the diet scale as the impairment increases. As the tendency at this stage is towards acidosis an alkaline ash diet is commonly advised. In our experience equally good results can be obtained by the administration of 30 to 60 gr. (2 to 4 gm.) of potassium citrate t.i.d. Fluid intake should no longer be restricted, as a greater excretion of water is necessary to compensate for the lessened power of concentration, otherwise blood nitrogen retention and uræmia must follow. A full salt intake should also be permitted, especially if vomiting is present, since there is a tendency at this stage to hypochloræmia. Such hypochloræmia further increases an already raised blood non-protein nitrogen and is itself a causal factor in the uræmic syndrome accounting for symptoms resembling those of adrenal failure such as somnolence, weakness and hypothermia. As œdema is not present at this stage, sodium chloride can be given. As hypertension is a feature of this stage of the disease, it may be wise to restrict food rich in purines, such as liver, sweetbreads and kidneys, as these are believed to have a pressor action. It is usually best to allow the patient to follow his



normal activities as far as possible, due regard being given to the state of his heart and general health (see p. 615). The end is inevitable and no point is served by withdrawing him from congenial employment until the condition forces it upon him. Any œdema present at this stage will be largely of cardiac origin and should be treated accordingly. The mercurial diuretics must be used with caution.

**Uræmia** is the natural termination in the majority of cases. While its onset may be inevitable, it frequently occurs earlier than need be owing to the presence of some other condition such as heart failure, prostatism, infections, gastro-intestinal disturbance or a superadded acute nephritis. A search for such precipitant causes should constantly be made and, if discovered, prompt treatment instituted. In most of them pre-renal loss of fluid into the tissues or by vomiting and diarrhœa leads to an insufficient circulation of fluid through the kidney, with resultant retention of products which would otherwise have been excreted. Eventually, however, no method succeeds in compensating for the impaired concentrating power and true uræmia arises. Gastro-intestinal symptoms develop insidiously and later nervous symptoms ensue associated with gradual onset of drowsiness and coma. Tetany may also occur as the result of the low calcium and raised phosphorus content of the blood.

The treatment of this type of uræmia is much less successful than that of the form occurring in the acute stage and is mainly of a symptomatic nature. Maintenance of hydration is of paramount importance. Abundance of fluid must be given. Venesection and lumbar puncture may give transient benefit when headache, fits and other cerebral signs are present. The beneficial results of these procedures are much less evident than in hypertensive encephalopathy. The intravenous administration of hypertonic solutions is of no service in chronic uræmia. Acidosis, as indicated by "uræmic asthma," may be counteracted to some extent by the intravenous administration of alkali. The alkalis should be given along with saline when, as commonly occurs, the chloride content of the blood is also low. For this purpose 30 to 50 c.c. of 8 per cent. solution of sodium bicarbonate should be given along with 500 c.c. of normal saline. Where latent or active tetany is present, calcium gluconate (10 c.c. 10 per cent. sol.) intramuscularly may be given two or three times a day. The gastro-intestinal symptoms are frequently most distressing, ulceration of the mouth, anorexia, vomiting and diarrhœa or constipation being the commonest. The vomiting and diarrhœa increase the pre-renal deviation of fluid, decrease the chloride content of the blood and increase the acidosis. They thus call for further intravenous administration of saline and alkali, and to these a weak glucose solution may be added (5 per cent.) to prevent the tendency to ketosis. Sedatives will be called for in all such cases: any may be given, even the morphine group. The danger of morphine in chronic kidney disease has been over-emphasized. It is now known that morphine has no detrimental effect on renal function. Since, however, excretion is seriously impaired, due care must be taken to guard against overdosage.

The artificial kidney, peritoneal dialysis and perfusion of an isolated intestinal loop are so restricted in their use that they only require mention here. They are of probable value in the true uræmia of first-stage nephritis, injury to the kidney, crush syndrome, anuria following transfusion of incompatible blood and operative treatment of kidney conditions.



## DIET I

MILK, GLUCOSE AND FRUIT-JUICE DIET FOR THE INITIAL STAGE OF  
ACUTE NEPHRITIS

(Protein content, 20 gm.)

(The glucose fruit-juice mixture is a 30 per cent. solution of glucose in water with the juice of 1 or 2 oranges or lemons added to each pint for flavouring purposes.)

- 8 *a.m.*—5 oz. citrated milk.  
 10 *a.m.*—5 oz. glucose fruit-juice mixture.  
 12 *noon*—5 oz. citrated milk.  
 2 *p.m.*—5 oz. glucose fruit-juice mixture.  
 4 *p.m.*—5 oz. citrated milk.  
 6 *p.m.*—5 oz. glucose fruit-juice mixture.  
 8 *p.m.*—5 oz. citrated milk.

*During Night*—5 oz. glucose fruit-juice mixture.

With improvement in the renal condition the milk can be wholly or partly replaced by a milk and cream mixture, while bread and butter, Benger's Food, arrowroot or other light cereals may be added.

When urea range lies between a maximum 1.5 to 2 per cent. (specific gravity below 1,018), place on Diet II. When the urea range shows a maximum concentration of 2.5 per cent. (specific gravity, 1,018), Diet III is given. With a maximum rise to 3 per cent. (specific gravity, 1,020+), Diet IV is used.

## DIET II

(Approximately 50 gm. protein)

*Breakfast*—

- |                                  |                          |
|----------------------------------|--------------------------|
| Grapefruit or orange with sugar. | Butter and marmalade.    |
| 2 oz. bread.                     | Tea with milk and sugar. |

*Forenoon*—

- 1 apple or orange, if desired.

*Dinner*—

- |  |                                       |
|--|---------------------------------------|
| 2 oz. meat or 2½ oz. fish.                         | Cereal pudding with milk from ration. |
| Large helping of vegetable (except peas or beans). | Stewed, tinned or fresh fruit.        |
| Average helping of potato.                         |                                       |

*Tea*—

- |   |                          |
|---|--------------------------|
| 1½ oz. bread.                                 | Butter and honey or jam. |
| Tomato, cress, lettuce, cucumber, if desired. | Tea with milk and sugar. |

*Supper*—

- |              |         |                            |
|--------------|---------|----------------------------|
| 2 oz. bread. | Butter. | Glass of milk from ration. |
|--------------|---------|----------------------------|

*Daily Rations*—

- |             |              |               |
|-------------|--------------|---------------|
| 2 oz. meat. | ¾ pint milk. | 5½ oz. bread. |
|-------------|--------------|---------------|

Two tea biscuits may be taken in place of ½ oz. bread, as far as their protein content is concerned.

## DIET III

(Approximately 75 gm. protein)

*Breakfast—*

6 tablespoonfuls porridge with	Butter.
milk from ration.	Marmalade.
1½ oz. bread.	Tea with milk and sugar.

*Forenoon—*

1 apple or orange, if desired.

*Dinner—*

3 oz. meat or 4 oz. fish.	Cereal pudding with milk from
Large helping of vegetables (except	ration.
peas and beans).	Stewed, tinned or fresh fruit.
Average helping of potato.	

*Tea—*

2 oz. bread.	Butter and honey or jam.
Tomato, lettuce, cress, cucumber,	Tea with milk and sugar.
if desired.	

*Supper—*

1 egg or ¾ oz. cheese; <i>or</i> , omitting	1 oz. meat at dinner, 2 oz. meat or
2½ oz. fish.	
2 oz. bread.	Glass of milk from ration.
Butter.	Fresh fruit if desired.

*Daily Rations—*

3 oz. meat.	1 pint milk.
1 egg.	6 tablespoonfuls porridge.
5½ oz. bread.	

One and a half ounces bacon, *or* 1 egg+1 oz. milk, may be substituted for 6 tablespoonfuls porridge.

Two tea biscuits, *or* ½ oz. spongecake, may be substituted for ½ oz. bread.

## DIET IV

(Approximately 96 gm. protein)

*Breakfast—*

6 tablespoonfuls porridge with	Butter.
milk from ration.	Marmalade.
1 egg.	Tea with milk and sugar.
1½ oz. bread.	

*Forenoon—*

1 apple or orange, if desired.

*Dinner—*

2½ oz. meat or 3 oz. fish.	Cereal pudding with milk from
Large helping of vegetables (except	ration.
peas and beans).	Stewed, tinned or fresh fruit.
Average helping of potato.	

*Tea—*

2 oz. bread.	Butter and honey or jam.
Tomato, lettuce, cress, cucumber, if desired.	Tea with milk and sugar.

*Supper—*

2 oz. meat or 2½ oz. fish.	Glass of milk from ration.
2 oz. bread.	Fresh fruit, if desired.
Butter.	

*Daily Rations—*

4½ oz. meat.	1½ pints milk.
1 egg.	6 tablespoonfuls porridge.
5½ oz. bread.	

One and a half ounces bacon, *or* 1 egg+1 oz. milk, may be substituted for 6 tablespoonfuls porridge.

Two tea biscuits, *or* ½ oz. spongecake, may be substituted for ½ oz. bread.

## DIET V

## FOR CHRONIC NEPHRITIS WITH ŒDEMA

(Approximately 130 gm. protein, low salt)

*Breakfast—*

2 eggs or 2 oz. fish (unsalted).	Marmalade.
2 oz. bread.	Tea with milk and sugar.
Unsalted butter.	

*Forenoon—*

Glass of milk from daily ration.

*Dinner—*

4 oz. meat or 5 oz. fish (unsalted).	Cereal pudding with milk from
Average helping vegetables (except	ration.
peas and beans).	Stewed, tinned or fresh fruit.
Average helping of potato.	

*Tea—*

2 oz. bread.	
Salad now or at supper, with 1 hard-boiled egg, <i>or</i> egg may be used in cooking, <i>i.e.</i> , in cereal pudding.	
Unsalted butter and honey or jam.	Tea with milk and sugar.

*Supper—*

4 oz. meat or 5 oz. fish (unsalted).	Glass of milk from daily ration.
2 oz. bread.	Fresh fruit, if desired.
Unsalted butter.	

*Daily Rations—*

8 oz. meat.	1½ pints milk.
3 eggs.	6 oz. bread.

All food to be prepared without salt.

No salt allowed with meals.

J. D. S. CAMERON.

## HYDRONEPHROSIS

In hydronephrosis there is dilatation of the renal pelvis and calyces with non-infected urine. If the urine becomes infected the condition of pyonephrosis is established.

Hydronephrosis may be congenital or acquired. The congenital form arises in connection with various developmental anomalies affecting not only the kidney but also the lower parts of the urinary tract. It sometimes arises without any anatomical abnormality being visible, and it is presumed in such cases to be due to a neuromuscular inco-ordination of the same type that gives rise to megacolon and hypertrophic pyloric stenosis.

The acquired forms of hydronephrosis arise as a result of obstruction to the urinary flow and may be unilateral or bilateral. The chief causes are blocking of the urinary tract by stone, neoplasm or inflammatory products (*e.g.*, renal tuberculosis; ureteric stricture; pressure on the ureter from without by tumours, inflammatory masses or adhesions; torsion of the ureter when the kidney is abnormally movable). These conditions usually give rise to a unilateral hydronephrosis, but may affect both kidneys. Bilateral hydronephrosis is, however, more commonly due to obstruction to or occlusion of the lower parts of the urinary tract (*e.g.*, neoplastic or inflammatory masses in the bony pelvis, urethral stricture, prostatic hypertrophy, phimosis or the presence of some mass such as a calculus in the bladder). If the obstruction to the urinary flow is intermittent, the conditions are favourable for a progressive increase in the degree of hydronephrosis, while a permanent obstruction leads to a more rapid destruction of renal tissue from pressure, so that the hydronephrosis tends to become stationary.

Minor degrees of hydronephrosis, such as occur in cases of generalized visceroptosis, may give rise to no symptoms and require no special treatment except when periods of exacerbation due to kinking of the ureter (Dietl's crises) cause pain and sometimes also vomiting and collapse.

Large or progressively enlarging dilatations of the renal pelvis may require surgical interference to remove the cause of the obstruction, and in every case where hydronephrosis is diagnosed or suspected a thorough urological examination should be made in order to determine (*a*) the cause and (*b*) whether the obstruction is unilateral or bilateral. Where no cause for the hydronephrosis is found that can be dealt with by operation, certain palliative measures may be employed. An intermittent hydronephrosis that is not giving rise to any serious symptoms can be left alone, but the patient should be kept under careful observation. A hydronephrosis that is associated with generalized visceroptosis may sometimes be prevented from developing acute obstructive phases by controlling it with a surgical belt, but the fitting of these appliances in women of the nervous type, who are usually the subjects of visceroptosis, is often a matter of difficulty. A simple arrangement of pad and binder may be more comfortable than one of the more elaborate and rigid forms of belt. Patients of an introspective type seem to find relief from wearing a support even when there are no acute symptoms. The measures described for the treatment of visceroptosis (see p. 566) are applicable to these cases. When a Dietl's crisis threatens or develops the patient should be put to bed, heat should be applied to the loins and a sedative such as 1 gr. (0.06 gm.) of phenobarbitone twice daily

should be given in conjunction with 15 minims (1 c.c.) of the tincture of belladonna thrice daily to diminish any tendency to spasm and achalasia of the ureteric sphincters. If pain is severe, however, morphia or pethidine may be necessary. In hydronephrosis associated with visceroptosis or "floating kidney" operative treatment should be avoided.

When there is an obstruction to the urinary flow that for any reason cannot be dealt with by operation, it is sometimes possible to relieve the pressure on the kidney tissue by ureteric catheterization, but this procedure should not be adopted without careful consideration of the nature and extent of the obstruction. If there is likely to be any risk of carrying infection into the renal pelvis from the lower parts of the tract the procedure should be avoided. Rest and the administration of belladonna in the doses indicated may be sufficient to relieve an exacerbation of the hydronephrosis by diminishing spasm. Prolonged pressure on the renal parenchyma by the retained fluid will ultimately lead to loss of function in the glomerular apparatus so that renal insufficiency results. This must be treated on the lines indicated for the treatment of chronic nephritis with renal failure (see p. 782). When infection occurs in a hydronephrosis a much more serious condition arises. It is important, therefore, to avoid instrumental interference as far as possible and to treat promptly any slight bacilluria or pyuria that may arise (see below).

It should scarcely be necessary to mention the need for testing the efficiency of each kidney separately if nephrotomy or nephrectomy is contemplated.

## INFECTIONS OF THE URINARY TRACT

The management of a case of infection of the urinary tract depends not only on the particular part most affected but also on the age of the patient and the type of infecting organism. There are, however, certain principles which are of general application. The term "pyelitis" is frequently used in a broad sense to include not only suppurative inflammation of the renal pelvis but also the associated inflammation of the ureter and bladder. It must not be forgotten that there may also be an extension of the inflammatory process into the tubular system of the kidney so that a pyelonephritis is produced.

Pyelitis may be acute, subacute or chronic. It may develop insidiously or come on suddenly without prodromal symptoms. In many cases the infection attacks a previously healthy urinary tract, but in others its development is favoured and its duration prolonged by the presence of some abnormality, such as congenital or acquired malformations, calculus, tumour or tuberculosis. It is important to make certain that there is no factor of this kind underlying the infection before embarking on prolonged courses of urinary antiseptics. It is obviously futile to attempt the treatment of an infected urinary tract with antiseptics alone when some obstruction to the free flow of urine exists, but this mistake is nevertheless a common one.

Apart from local abnormalities in the genito-urinary organs there are many general conditions which predispose to the occurrence of urinary infection. Common causes of this type are influenza, the state of lowered resistance that follows the exanthemata, the cachexia of chronic renal or cardiac disease, malignant disease or tuberculosis. Chronic constipation,

colitis, diverticulitis, anal fissure and infected hæmorrhoids are frequently factors in the development of urinary infections—particularly with organisms of the coliform group. In all cases of urinary infection with *Bacillus coli*, therefore, a careful examination should be made to exclude such pathological conditions in the large bowel, which should receive appropriate treatment if found to be present.

Pyelitis is common in pregnancy, and in this state there are mechanical factors, with dilatation of the ureter and achalasia of the ureteric sphincters, which are favourable to the growth of organisms on account of the stagnation of the urinary flow to which they give rise. In young persons, and in middle-aged adults who have no pre-existing disease of the urinary tract, the infection usually gives rise to a pyelitis with only a moderate inflammatory reaction in the kidney and in the lower part of the urinary tract. In elderly subjects the bladder infection is often the most troublesome feature and is most resistant to treatment. The deformed bladder of the elderly man with prostatic hypertrophy forms a favourable site for the continued activity of the infecting organisms which grow in the residual urine that is left behind after the incomplete evacuation of the bladder. Similar factors favour the continued growth of organisms in the bladders of women with uterine prolapse and cystocele.

In the acute form of pyelitis there is often a very severe general disturbance from toxic absorption. In the early stages the febrile reaction and its accompanying symptoms may be so prominent that the existence of an infection of the urinary tract may be overlooked if the examination of the urine is not properly carried out. In severe cases there is high fever with rigors, headache, lumbar pain and general prostration. Signs of bladder irritation, though often present, may be so indefinite as to be overlooked. This is particularly likely to occur in children who are unable to describe their symptoms accurately.

The essential point in the diagnosis of infections of the urinary tract is the demonstration of pus and organisms in the urine. Pus may be so abundant as to be obvious on casual inspection of the urine, but is frequently scanty in amount, and its presence can then be detected only by microscopic examination. The old-fashioned test with liquor potassæ ("ropiness" when the reagent is added to the urine) is of no value. When it is positive, the amount of pus present is usually sufficient to be visible to the naked eye. Absence of "ropiness," on the other hand, is no indication of the absence of pus or bacilluria. It must be emphasized, therefore, that the only reliable way of ascertaining whether pus and organisms are present in the urine is by microscopic examination. If there is any question of contamination of the urine—as, for example, by the vaginal discharges—it is necessary to obtain a catheter specimen. Even where this is not considered necessary it is well to allow the first part of the bladder contents to be evacuated before the specimen for examination is collected. In this way confusion will be avoided between a true pyuria or bacilluria and contamination of the urine with pus from the urethra or genital passages.

If any appreciable amount of pus is present it will be seen in a fresh wet preparation of the urine examined under a low or medium power lens. If the urine is examined after centrifugalization it must be remembered that a normal urine may show a few leucocytes in the deposit and that this must be taken into account in interpreting the results and correlating it with

the clinical findings. As a criterion of the results of treatment, culture of the urine is commonly made, and it is frequently found that after a successful course of medication the urine has become sterile. This does not necessarily indicate, however, that there is no residual nidus of infection which may again become active when the antibacterial action of the drug is withdrawn.

A great variety of organisms may be found in urinary infections, but the commonest is the group of coliform bacilli. *B. coli* may occur as a pure infection or as part of a mixed infection along with enterococci or streptococci. *B. proteus* is an important infective agent on account of its strong urea-splitting action which gives rise to an alkaline ammoniacal urine and necessitates special precautions in treatment. Certain of the coccal infections (streptococcal and staphylococcal) involve the same difficulty, though in less marked degree than *B. proteus*. Urea-splitting with ammonia formation does not occur to any extent with *B. coli* and the paratyphoid group, so that control of urinary reaction in these infections is simplified.

Care should be taken that an underlying infection with *B. tuberculosis* is not overlooked. If there is any reason to suspect its presence the appropriate methods of searching for it should be applied, and it should not be assumed that because there is a heavy infection with a coliform or coccal organism the whole bacteriological picture has been established. Since non-pathogenic organisms, particularly coliform bacilli, may multiply at room temperature in a specimen of urine, the true cause of a urinary infection may be missed if there is delay in examining the specimen.

In the investigation of a case of infection of the urinary tract it must be remembered that the fundamental cause of the condition may be some abnormality or disease outside the genito-urinary system. It is necessary, therefore, if a satisfactory course of treatment is to be laid down, that a full general examination of the patient should be made. In many cases it is futile to attempt to overcome the infection by giving urinary antiseptics without also dealing with the following factors should they be present: (1) malnutrition, due to an insufficient or improperly balanced diet; (2) lowered resistance, due to some metabolic disorder such as diabetes mellitus; (3) chronic intoxication from a diseased appendix or from some lesion of the gastro-intestinal tract such as colitis, diverticulitis, inflamed hæmorrhoids, fistula or carcinoma; (4) anæmia, whether it be nutritional, post-hæmorrhagic or dyshæmopoietic in type; and (5) mechanical or nervous causes leading to interference with the regular or complete emptying of any part of the urinary tract.

**General Management of the Patient.**—Having diagnosed the presence of infection of the urinary tract, the first point to decide is whether the patient may be treated as an ambulatory case or must be confined to bed. In all cases where the infection is acute, and in most cases where it is subacute, rest in bed is essential. The need for this is clear in severe cases with general febrile and toxic manifestations, but it may not be so obvious to the patient when the infection is only subacute. It should be explained to him that his recovery is likely to be much quicker if he submits to a period of complete rest. After the fever has settled and the toxæmia has subsided, the patient may be allowed up for short periods as this helps to promote drainage, but he must not be allowed to expose himself to chill and should avoid exertion until convalescence is well established.

Regulation of the bowels is important, as in many cases chronic con-

stipation is present. A soap and water enema (1 oz. of green soft soap to each pint of warm water) should be given and may be repeated daily. In some cases an olive oil enema may be required to dislodge inspissated faeces (10 oz. of warmed olive oil run in, under gravity, through a rubber catheter). It is undesirable to give cathartics as their action may tend to encourage the migration of coliform organisms through the gut wall, but the regular evacuation of the bowels should be secured by giving small doses of cascara and belladonna.

**Diet.**—During the acute febrile stages of pyelitis the diet should be restricted to water, glucose, fruit juices and diluted milk. As soon as the toxæmia shows signs of clearing, light farinaceous foods, bread and butter, toast, or plain biscuits may be added to the diet. With further improvement, egg and fish dishes and vegetable purée may be allowed. When the method of treatment adopted does not necessitate the restriction of fluid, large quantities of milk may be allowed, either fresh milk, buttermilk, or milk shakes (that is, milk flavoured with fruit syrup). The quantities of food may be gradually increased, but until convalescence is definitely established these dietary restrictions should be continued. Reference is made below to certain forms of treatment which necessitate a restriction of the fluid intake, and to others in which the amount of fluid must be increased above the normal. The dietary management of the patient must be modified according to which of these methods is chosen.

**Control of Pain and Pyrexia.**—Apart from irritation in the bladder and urethra, severe pain is not usually a prominent feature in pyelitis, but there is often a good deal of dull aching and discomfort in the abdomen and in the lumbar region. This pain may respond to the local application of heat by means of rubber hot-water bottles, a hot compress or an electrically heated pad. It may also be alleviated by a simple analgesic such as the following:—

Acid. Acetylsalicyl.	. . . . .	gr. v. (0.3 gm.)
Phenacet.	. . . . .	gr. iii (0.18 gm.)
Codein. Phosph.	. . . . .	gr. $\frac{1}{2}$ (10 mg.)

General mild sedation with  $\frac{1}{2}$  gr. (0.03 gm.) of phenobarbitone three or four times a day may be found useful in the early stages of an attack. When pain is severe the ideal analgesic and antispasmodic in this condition is pethidine hydrochloride, which may be given orally or hypodermically in doses of 50 to 100 mg.

Pyrexia is best controlled by tepid sponging, but care should be taken to avoid chilling the patient by exposing large areas of the body surface. If the analgesic mixture of aspirin, phenacetin and codeine referred to above is being used it will tend to lessen the fever.

**Alkalis.**—The reaction of the urine in pyelitis may be either acid or alkaline. In the common form of infection with coliform organisms, the urine is acid unless it has been lying in the bladder or other part of the urinary tract for a sufficient time to allow of decomposition. A great deal may be done to inhibit the growth of organisms by altering the reaction of the urine so that it is unfavourable to them. Artificially induced changes in the reaction in the urine slow down the rate of growth of organisms. These changes in reaction can be brought about very easily if the dosage of the drugs used is properly adjusted, but if the amounts given are inadequate they will fail to produce any improvement. In the common form of urinary tract infec-



tion, with a highly acid urine, the aim is to produce a sudden change to alkalinity. This can be done by giving sufficient amounts of potassium citrate, sodium acetate or sodium bicarbonate. If it is desired to change an alkaline urine to an acid one, the most suitable drugs to employ are ammonium chloride or sodium acid phosphate. Reference is made below to the use of these acidifying drugs in connection with mandelates. The alkaline diuretic treatment, in addition to inhibiting the growth of many of the common types of organisms, has a beneficial effect in other ways. By producing a large amount of dilute non-irritating urine it minimizes local irritation and mechanically flushes out the urinary passages. In many cases the administration of alkalis alone will be followed by an arrest of the infective process, but it is desirable to combine it with one of the sulphonamides (see below). Failure to obtain good results with the alkaline method is generally due to inadequate dosage or to failure of the patient to co-operate. The first essential is to make sure that the patient is taking large amounts of fluid. A minimum of 5 pints of water—alone or combined with barley water, fruit drinks, tea, or diluted milk—should be insisted upon. The intake should be spread as evenly as possible over the twenty-four hours, so that at no time does the urine become highly concentrated. The output of urine following this intake should be somewhere in the region of 100 oz., and if the diuretic response is unsatisfactory the fluid intake may be further increased. Failure to obtain a sufficient output of urine is generally due to the patient not having carried out the instructions with regard to fluid intake.

The amount of alkali to be given depends to some extent on the response of the patient. As much as 30 gr. (2 gm.) each of potassium citrate and sodium bicarbonate every two hours may be required for the first day or two. The reaction of the urine to litmus must be taken each time the bladder is emptied, and as soon as the urine becomes frankly alkaline the dosage may be cut down by giving the mixture only once every four hours. Some patients are very resistant and require larger doses for a longer period. Another very simple method of securing alkalization of the urine is to prescribe potassium citrate alone, in solid form, and to instruct the patient to take a teaspoonful (approximately 60 gr. or 4 gm.) every two hours until the litmus turns blue, and thereafter every four hours. Should he subsequently find the litmus failing to turn blue he should resume the two-hourly doses until the reaction is again adjusted. Occasionally patients object to the insipid taste of the citrate. This may be overcome by giving 6 minims (0.35 c.c.) of concentrated infusion of gentian in  $\frac{1}{2}$  oz. of water with each dose. Disodium hydrogen citrate is useful in cases where there is a tendency to nausea. The dosage is similar to that of the simple citrates. It is useless to continue the attempt to treat infection of the urinary tract by this method if the urine does not become alkaline. To prevent hypochloræmia from the free diuresis, 1 to 2 drachms (4 to 8 gm.) of sodium chloride should be included in each day's diet.

If the alkaline diuretic treatment is carried out in the manner described, pyuria may be expected to diminish within a few days and may even clear up completely, but the duration of the treatment is lessened and the cure is more effective if this régime is combined with the administration of sulphonamides (see below).

**Urinary Antiseptics.**—*The Sulphonamides.*—The introduction of the sulphonamide group of drugs has given us a potent weapon in the treat-

ment of infections of the urinary tract. The different types of sulphonamide preparations have been discussed in detail on p. 71 *et seq.* It is as yet premature to say dogmatically which of these drugs will prove to be the most effective in dealing with the varying infections which may occur in the urinary tract. As the activity of these preparations varies with different types of infection, it is an advantage to know the bacteriology of the urine in order that the most economical use may be made of the drug selected. Where there are no facilities for an immediate bacteriological diagnosis, sulphathiazole or sulphadiazine are recommended as the most generally useful of the group.

In treating an infection such as pneumonia with drugs of the sulphonamide group the aim should be to raise the concentration of the drug in the blood and tissues to the optimum level and to maintain it there. In applying these drugs to the treatment of urinary tract infections, however, it is not the concentration in the blood but the concentration in the urine that is important. It should be remembered that when there is impaired renal efficiency the rate of excretion of the sulphonamide may be so slow that an effective concentration of it in the urine is difficult to obtain. Further, the concentration in the blood is proportional to the dosage (assuming the rate of absorption to be normal), while the concentration in the urine may be kept below the effective level by excessive diuresis.

It is desirable in the acute stages of pyelitis to maintain a high output of urine, and during this part of the treatment it may be necessary to give a larger dose of the sulphonamide to compensate for the dilution effect of the diuresis, while in the later stages of the illness, when the fluid intake can be more safely reduced, the dosage can be diminished without risk of losing its therapeutic effect.

In this connection it may be noted that when there is infection in the deeper structures (as in pyelonephritis, prostatitis and vesiculitis) the action of the sulphonamide depends upon its concentration in the blood and tissue fluids as well as on its antibacterial action in the urine.

Further, if a high dosage of sulphonamide is continued for more than a week at a time there is a tendency for deposits of an acetyl derivative to form in the kidney, where they may cause blockage of tubules and even of the ureters (the calculi, being translucent to X-rays, may be undetected). Apart from the danger of toxic action, this is an additional reason for keeping the dosage down to the lowest effective level.

There is no definitive rule as to the dosage of the sulphonamides in urinary infections. The average effective dose for an adult is 2.5 to 3 gm. per diem given in doses of  $\frac{1}{2}$  gm. ( $7\frac{1}{2}$  gr.) four-hourly. Five to 6 gm. may be given during the first day in order to bring about a rapid rise in the concentration of sulphonamide in the blood, but the smaller dose is sufficient to maintain a concentration in the urine at about 150 mg. per 100 c.c. of urine, which is high enough to be actively antibacterial.

The sulphonamide preparations have been used alone, but are more effective if combined with the alkaline diuretic treatment described above. In the writer's experience this combination has much to commend it and, particularly in infections with *B. proteus*, it has given very encouraging results. The beneficial effects of diuresis and of alkalization of the urine need not be sacrificed, while the additional antibacterial action of the

sulphonamide helps to reduce the time required for the sterilization of the urine. With this combined treatment there is a rapid diminution in fever and toxæmia, and it is common to find that not only does the pus disappear from the urine within a week or ten days but that the urine becomes sterile on culture.

*Mandelic Acid.*—About 1931 there was introduced a method of treating pyelitis by inducing a ketosis with a "ketogenic" diet in which the normal balance of carbohydrate and fat was upset by restricting the former and increasing the latter until ketonuria was produced. The method was troublesome to use and uncertain in action but seemed to contain a principle of some value. Investigation showed that  $\beta$ -hydroxy-butyric acid has a powerful action in preventing the growth of organisms if the urine is sufficiently acid (pH 5.3). Hydroxy-butyric acid cannot be given orally because it is destroyed in the upper part of the alimentary tract, but mandelic acid was shown by Rosenheim to be an effective substitute for it. The use of mandelic acid in infections of the urinary tract marked a striking advance, but since the introduction of sulphonamide treatment it has lost much of its importance. On account of the necessity for giving some additional drug to alter the reaction of the urine, and also because of the unpleasant and irritating effects of mandelic acid in the stomach, it is now customary to use one of the salts, such as sodium, ammonium or calcium mandelate.

In giving mandelic acid or one of its salts the reaction of the urine must be kept at or below pH 5.3. If the acidity should become less than this the antibacterial action of the mandelic acid is lost. When the fluid intake is restricted this degree of acidity may develop spontaneously, but if it does not, ammonium chloride must be given in addition. The common method of acidifying the urine for this purpose is to give 15 gr. (1 gm.) of ammonium chloride four times a day. In some cases this is insufficient to render the urine highly acid and multiples of this dose up to as much as 6 or 8 gm. may have to be used. Treatment with these large doses cannot be continued for long on account of the irritating effects of the ammonium chloride, and in some patients even the smaller doses are not tolerated. Preparations such as calcium mandelate and ammonium mandelate are on the whole less irritating and less nauseating. Though slightly more expensive, they are preferable to ammonium chloride and mandelic acid. It should be emphasized that unless the urine reaches the proper degree of acidity it is useless to attempt to continue the treatment with mandelates.

The usual basic dose of mandelic acid is 45 gr. (3 gm.) four times a day. The equivalent of this in the form of sodium mandelate is 50 gr. (3.24 gm.). If it is desired to use a non-proprietary preparation, the following mixtures are effective:—

#### No. 1.—AMMONIUM CHLORIDE MIXTURE

Ammon. Chlorid. . . . .	dr. $\frac{1}{2}$ (2 gm.)
Extr. Glycyrrh. Liq. . . . .	fl. dr. 4 (14.4 c.c.)
Aq. . . . .	to fl. oz. 8 (227 c.c.)

Sig.—One tablespoonful four times a day before food.

(Note.—Ammonium chloride may be given dry in cachets if preferred.)

## No. 2.—SODIUM MANDELATE MIXTURE

Sod. Mandelate . . . . .	fl. oz. $1\frac{1}{2}$ (43 c.c.)
Syr. Aurant. . . . .	fl. oz. $1\frac{1}{2}$ (43 c.c.)
Aq. . . . .	to fl. oz. 8 (227 c.c.)

Sig.—One tablespoonful four times a day after food.

The reaction of the urine must be tested regularly by adding 5 drops of a buffered solution of methyl-red to  $\frac{1}{2}$  in. of urine in a test-tube. At pH 5.3 the colour is bright pink, but above this the colour is orange or yellow, indicating that the urine is alkaline or not sufficiently acid. This indicator solution can be purchased ready for use. A number of drug manufacturers supply preparations of ammonium or calcium mandelate under proprietary names. These are more palatable and quite reliable, but are necessarily slightly more expensive than non-proprietary mixtures. Examples of these preparations are:—

*Ammoket*.—Dose, 4 drachms (14 c.c.) four times a day. Supplied by Boots Pure Drug Co. Ltd.

*Calcium Mandelate Compound*.—Dose 4.4 gm. four times a day. Supplied by Burroughs Wellcome.

*Mandecal*.—Dose, 4 to 5 gm. (1 level dessertspoonful four times a day). Supplied by British Drug Houses Ltd.

*Mandelix*.—Dose, 2 drachms (7 c.c.) four times a day. Supplied by British Drug Houses Ltd.

*Neoket* (mandelic acid, sodium bicarbonate and sodium acid phosphate without ammonium chloride).—Dose, 2 drachms (7 c.c.) four times a day. Supplied by Boots Pure Drug Co. Ltd.

When one of these preparations is given the reaction of the urine usually reaches the proper degree of acidity, but if there is failure to get a pH 5.3, doses of 10 gr. (0.6 gm.) of ammonium chloride may be given three or four times a day until the reaction is corrected. There are exceptionally resistant cases, but usually, if the mandelic acid treatment is carried out carefully, the urine becomes sterile within seven to ten days unless there is some anatomical abnormality such as a deformed bladder or a renal calculus. An undesirable point about the treatment with mandelic acid and its derivatives is the necessity for some restriction of the fluid intake, and in cases where there is renal disease the drug may produce irritation of the kidneys. If signs of such irritation should appear, *e.g.*, hæmaturia, gross albuminuria, or a heavy deposit of casts, the drug should be stopped and one of the other methods of treatment substituted. On account of its tendency to cause irritation, and because of the necessity of restricting the fluid intake, it is undesirable to use mandelic acid in the acute phase of pyelitis or in the presence of severe pyelonephritis. When the patient is febrile and toxic, the alkaline diuretic method alone or in conjunction with sulphonamide should be used until the acute phase has passed off.

*Penicillin*.—Most strains of *B. coli* are insensitive to penicillin. It is not yet established how far penicillin is likely to replace other forms of treatment when the infection is due to an organism sensitive to penicillin. Parenteral administration has given promising but not conclusive results in the treat-

ment of recent infections due to such organisms, but in more chronic cases any improvement obtained seems to be only temporary and relapses tend to occur as they do after the older forms of treatment. (For dosage and method of administration see p. 86.)

*Hexamine, Pyridine and Hexyl-resorcinol* have all been extensively used in urinary infections. They are, however, inferior as urinary antiseptics to the sulphonamides and mandelates and are not to be recommended.

**Drainage of the Ureter.**—In some cases of pyelitis, particularly in those associated with pregnancy, there is difficulty in maintaining satisfactory drainage of pus from the renal pelvis. One factor interfering with drainage is achalasia of the ureter and this may to some extent be overcome by giving atropine, but it may be impossible, even with full atropinization and free diuresis, to overcome the tendency to stagnation of urine and accumulation of pus in the ureter and renal pelvis. If this natural process of lavage is insufficient to clear the tract it is occasionally necessary to catheterize the ureters and wash out the renal pelvis. For this purpose acriflavine (1 : 5,000) or silver nitrate (1 : 5,000) may be used. The procedure requires special technique and experience and should only be carried out by a urologist. The writer has sometimes seen striking improvement after such lavage when the ureteric catheters were left in position for twenty-four hours to establish drainage. These periods of recurrent blocking of the ureter are usually associated with an increase in toxæmia and pyrexia, and the fact that the hold-up may cause a temporary diminution of the pus in the urine may lead to difficulty in diagnosis.

Lavage of the bladder is sometimes the most effective way of dealing with the residual cystitis which is found particularly in elderly people who have had an acute infection of the urinary tract or an acute or subacute exacerbation of a chronic infection. Bladder lavage may be carried out daily, or on alternate days, for one to two weeks and after that at longer intervals. A non-irritating fluid should be used such as normal saline, boracic lotion, 1 : 5,000 acriflavine or 1 : 10,000 silver nitrate. After the bladder has been washed out and emptied, 10 c.c. of 10 per cent. mild silver protein may be injected into it just before the catheter is withdrawn.

### SUMMARY

In the initial stages of acute pyelitis when there is fever and general toxæmia, the most satisfactory treatment is the diuretic alkaline régime. Sulphathiazole or one of the other sulphonamides may be given in suitable doses in combination with this. Until all signs of general disturbance have settled down the patient must be kept at rest in bed in a room kept at an equable temperature, and his activities should be restricted for some time thereafter. In the majority of uncomplicated cases pus will have disappeared and the urine will have become sterile on culture within ten days. If the infection persists, one of the mandelate preparations should be used unless there is some contraindication such as active renal disease. It is only rarely that drainage and lavage of the renal pelvis is required, but bladder lavage is frequently useful in overcoming a residual cystitis. Penicillin appears to have a place in the treatment of acute infections of the urinary tract due to penicillin sensitive organisms, but its exact value has not yet been assessed.

It cannot be emphasized too strongly that in the application of most of these methods of treatment the regulation of the reaction of the urine is of great importance. Unless attention is paid to this point the results are likely to be unsatisfactory and the course of the illness unduly prolonged. Further, it is of paramount importance to make sure that no obstructive lesion, stone or underlying tuberculous disease is present in the urinary tract, and to treat any pathological condition which may be present in the colon.

## RENAL CALCULUS

While the radical treatment of renal calculus is a surgical matter, there are many points in the management of the patient that are the concern of the physician. In cases where there is an excess of those constituents of the urine that tend to form calculi, certain dietary and medical measures may lessen the formation of crystalline deposits and so minimize the risk of calculus formation. Again, renal colic, hæmaturia, anuria and the infection of the urinary tract that so frequently accompanies renal calculus are all amenable to medical treatment.

In the past, various medicinal and dietary measures have been prescribed for the prevention and treatment of urinary stone, but in the light of more recent clinical and metabolic studies it seems very doubtful how far these are likely to be effective. Calculi may be formed from normal or from abnormal urinary constituents. In the case of the former, the more common substances are uric acid, calcium oxalate and phosphates. It has been found in animal experiments that the level of these substances can be raised far above the concentrations that occur in man without any formation of calculus, and the general inference is that there must be some epithelial or other damage to the urinary tract before calculus formation of this kind occurs. Even in the case of calcium oxalate, which may appear in crystalline form when articles of diet rich in oxalate are taken in excess, it has been found that urine will retain in solution three or four times as much as can be dissolved in the same volume of water. Similarly, in the case of uric acid, which is generally believed to form calculi in response to an excessive intake of purines, ten to twenty times as much will remain in solution.

Any patient who is threatened with renal calculus, whether he has signs of actual calculus or has merely been passing gravel or crystalline accumulations, should be given large quantities of fluid. In many cases it will be found that he has been habitually taking less fluid than his normal requirements, but whether this is the case or not he should be instructed to take a definite volume of fluid every day. Water, barley water, lemon drinks such as *potus imperialis* may be prescribed, or one of the natural mineral waters may be ordered. It does not matter very much which is used so long as the volume of fluid is adequate, that is, 4 to 5 pints in the day. If there is an abnormal concentration of urates, uric acid or oxalates in the urine, alkali should be given in moderate doses. The large doses used in the treatment of pyelitis are not required, but 20 to 30 gr. (1.2 to 1.8 gm.) of potassium citrate three times a day may be continued for months at a time. If the urine is kept strongly alkaline there may be a tendency to the deposition of phosphates round a pre-existing oxalate or uric acid stone, so that care should be taken to keep the reaction of the urine just on the alkaline side by

suitable regulation of the dosage of citrate. If there is any tendency to colic or irritation, 15 minims (1 c.c.) of tincture of belladonna should be given three or four times a day for two or three days. This short course may be repeated from time to time as required. In such cases it is particularly important to make sure that the patient is taking a large amount of fluid so as to keep the urine dilute and non-irritating. Incidentally, the administration of belladonna and the production of a free diuresis and general relaxation by means of hot drinks and a hot bath may be followed by the passage of small calculi which would otherwise have remained impacted in the urinary tract.

Since phosphatic deposits occur in an alkaline medium, care should be taken to keep the urine faintly acid if there is known to be a tendency to the formation of phosphatic calculi. The fluid intake must be liberal, as in dealing with other forms of calculi, and 10 gr. (0.6 gm.) of sodium acid phosphate four-hourly may be given if necessary to control the reaction of the urine.

Regulation of the diet has always been considered desirable if there is any tendency to the excretion of excessive amounts of uric acid or urates in the urine, and it has been supposed that the amount of meat, eggs and other sources of animal protein should be cut down and the patient instructed to take a liberal amount of fruit and vegetables. All substances rich in nucleo-proteins, *e.g.*, kidney, liver, sweetbreads and beef, and also such purine-rich beverages as tea and coffee, are usually recommended to be reduced to a minimum. In general, the dietary restrictions are those recommended in the treatment of gout (p. 851). The efficacy of such restrictions is doubtful, and it should be noted that in parts of India and China, where the ordinary diet is very poor in purine-containing elements, the incidence of uric acid stone is high.

When the patient's circumstances permit, a course of treatment at a spa is often an effective prophylactic measure, but if the patient is willing to co-operate fully in the treatment there is no real advantage in putting him to the trouble and expense of giving up his ordinary duties and leaving home.

**Renal Colic.**—Renal colic occurs when a calculus enters the ureter or when the ureter is attempting to pass it into the bladder. Severe pain may also arise after a calculus has entered the bladder or while it is passing along the urethra. The pain of renal colic is of such a commanding nature that prompt measures are necessary for its relief. The most effective drug for this purpose is morphine. A  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (16 to 32 mg.) should be given in combination with  $\frac{1}{100}$  gr. (0.6 mg.) atropine sulphate, and this injection of morphine and atropine may be repeated at intervals of three or four hours until the severity of the pain is controlled. In some cases it may be necessary to give inhalations of chloroform to obtain relief from the agonizing pain until the morphine has had time to act.

After the attack of colic has passed off the patient should be kept in bed for a few days and the urine should be examined daily for blood and pus. Even if no pus is found it is well to give a course of urinary antiseptic treatment as a prophylactic. If there is reason to suspect that the calculus is of the type that forms in acid media, citrate should be given in the doses indicated above, while in the other type of case with a tendency to phosphatic deposits the urine should be kept acid by the use of ammonium chloride or dilute hydrochloric acid.

In the majority of cases where there is a calculus of considerable size, surgical treatment will be necessary sooner or later, but the management of the patient before and after the operation should be along the lines indicated. Particular care must be taken to diminish the risk of infection of the urinary tract, and if it does develop it should be treated in one of the ways described in the section devoted to that subject.

### PHOSPHATURIA

Normal urine contains large amounts of phosphate, and the formation of a deposit of phosphates when the urine is amphoteric or alkaline is not an indication of disease. Some people, however, tend to excrete an unusual amount of phosphate. They are usually taking large amounts of fruit and vegetables in their diet. Phosphaturia is also found in patients with hyperchlorhydria and in nervous and debilitated people with muscular wasting. There appears to be some relationship between the formation of stone in the urinary tract and vitamin A deficiency. If this is so, then it is likely to be because of the effect of such deficiency on epithelial nutrition, but it seems improbable that this is a common factor, as gross vitamin A deficiency is relatively rare.

It is doubtful whether excessive concentration of phosphates in the urine can be dissipated by diminishing calcium-rich foodstuffs such as milk, eggs and vegetables and increasing the amount of meat, cereals and potatoes, as was at one time supposed. Phosphaturia occurs also in association with cystitis when there has been ammoniacal decomposition of the urine. This is seen commonly in the common form of cystitis that accompanies prostatic hypertrophy. It usually clears up when the cystitis is treated by one of the methods described in the section on infections of the urinary tract.

### OXALURIA

Oxaluria is a condition in which crystals of calcium oxalate appear as a deposit in the urine. The oxalates are derived usually from foodstuffs rich in these salts. These are mainly such vegetables or fruits as spinach, rhubarb, tomatoes and strawberries. Oxaluria may occur when such articles of diet are taken in large amounts, and it is believed that individuals with a highly acid gastric secretion are particularly prone to develop oxaluria, when these forms of fruit or vegetable food are taken in excess. The oxalate crystals may cause irritation and pain and there may even be some degree of hæmaturia. Sometimes signs of general disturbance are found, such as headache, dyspepsia and lassitude. Oxalate calculi may form—the so-called “mulberry stone.” These give rise to the usual symptoms of renal or ureteric calculus.

The main point in the treatment of oxaluria is the restriction of all articles of diet that are rich in oxalates. In addition to the fruits and vegetables mentioned above, it is necessary to restrict the use of tea and cocoa, since these contain oxalate. Milk, eggs, sugar, butter, wheatmeal and rice may all be allowed with safety, as they are the foodstuffs least likely to lead to a persistence of oxaluria, and magnesia can be given daily in the form of magnesium sulphate or carbonate.

J. N. CRUIKSHANK.



# CHRONIC RHEUMATIC DISEASES

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## INTRODUCTION

**T**HE rheumatic diseases, both acute and chronic, are, for the most part, diseases of temperate climates. In countries enjoying this mixed blessing they constitute a serious menace to the health and well-being of the community. Only within recent years have statistics been compiled which indicate the magnitude of the problem. It is officially admitted that one-sixth of the total annual invalidity of insured persons in Great Britain is due to rheumatic disease in one or other of its forms. In Scotland, with a population of approximately 5 million, 50,000 insured persons are totally incapacitated annually, for an average period of sixty days. Investigations carried out by the writers indicate that at least 300,000 new cases of rheumatic disease requiring medical treatment occur annually in Scotland, of which about 75 per cent. belong to the group of fibrositic diseases affecting muscles, nerves and tendons. Such figures give some indication of the enormous economic loss resulting from the ravages of this group of diseases, and of the vast amount of pain and misery entailed.

When the section on treatment has been perused, it will become clear that many of the complex and specialized measures required for diagnosis and treatment are outside the scope of general medical practice, and it is officially admitted that there is an urgent need for the provision of special facilities for the treatment of the more chronic forms of rheumatic disease. It is for these reasons that we advocate most strongly the establishment of a national scheme for the control and treatment of the chronic rheumatic diseases, the essential feature of which would be the provision in selected areas throughout the country of clinics in charge of physicians who have received special post-graduate training, and who would decide whether patients suffering from chronic rheumatic disease should be treated by the family physician at home, at the treatment centre as out-patients or in hospital. Only by accurate diagnosis in the early stages of the more severe forms, and by the immediate institution of the proper lines of treatment, can the regrettably common legacy of permanent incapacity be reduced or avoided. The problem of ætiology is so complex, that for its elucidation the physician must have at his disposal the help of a team of specialists in all branches of medicine, by whose concerted efforts the problem of each individual case can be unravelled.

The Governments of Sweden, Russia and other Continental countries have accepted the fact that the chronic rheumatic diseases constitute a major cause of invalidity and have put into operation plans for the control of this scourge. It is to be regretted that this country has lagged behind many of her Continental neighbours in this respect.

Before any scheme of treatment is adopted for an individual patient, it must again be emphasized that accurate diagnosis of the type of rheumatic disease present is vitally important. To label a disease "rheumatism" and to prescribe analgesics is no longer justifiable in view of the great advances

in treatment which have been made during recent years. When a diagnosis has been reached, the next step is to estimate the degree of activity of the disease process. This is especially applicable to the rheumatoid or chronic infective type, where the disease may be encountered for the first time in the acute, subacute or chronic stage. Accurate knowledge as to the activity or otherwise of the disease processes is essential if treatment is to be applied in a rational manner. The measures adopted during the acute or active phase differ radically from those employed in the subacute or chronic state, and the use of over-strenuous measures at the wrong time may lead to disaster. To estimate the degree of activity on clinical grounds alone may present considerable difficulty. The local and general condition must be carefully considered. Determination of the sedimentation rate of the red blood cells should be carried out in every case of arthritis. The technique of this test is simple and should be undertaken by every family doctor who wishes to treat the more severe forms of chronic rheumatic disease. Accordingly the technique of the test is described on p. 849. Often, in an apparently quiescent case, the test will reveal a marked degree of activity indicating the possibility of a relapse, especially if too radical forms of treatment are employed. Repeated determinations of the sedimentation rate at weekly intervals throughout treatment serve as a useful index of the progress of the case. As the disease becomes quiescent the reading will gradually return to normal. It must be borne in mind, however, that this return lags considerably behind clinical improvement, and in the presence of an obvious change for the better in the patient's condition the importance of a rapid rate must not be overstressed as long as the tendency is for it to fall and not to rise.

When the physician has reached a correct diagnosis and has assessed the degree of activity present, the next step, before embarking on a scheme of treatment, is to institute a thorough search for ætiological factors, and it is at this stage that the aid of specialists, in the various systems where focal sepsis is prone to occur, must be invoked. Expert opinion is essential before the patient is condemned to lose his teeth, have his tonsils removed or sinuses drained, to quote one or two examples, but not infrequently the rôle of the practitioner will be to protect his patient from the over-enthusiasm of the specialist.

Many factors are believed to play a part in the ætiology of the different forms of chronic rheumatic disease—infection, environment, constitution, occupation, the anatomic type of the patient, impairment of the body mechanics, etc. In a particular case one factor may appear to dominate the picture. For example, a thorough soaking may precipitate an attack of lumbago, but the underlying cause may be a low-grade infection, or a metabolic disturbance secondary to faulty dietetic habits. The physician should remember that a healthy body has, until its vitality is impaired, a remarkable capacity for withstanding isolated insults offered to it by its environment externally and its owner internally. Accordingly, although the amelioration of pain is the first consideration both of the patient and his physician, the latter will not have fulfilled his obligations until he has made an effort to discover and remove the underlying cause and has thus restored to the body its ability to withstand the insults with which it will inevitably be faced.

The first consideration in the treatment of chronic rheumatic disease is to secure the co-operation of the patient. Chronicity is an essential feature

of the more severe forms of the disease, and unless the patient has full confidence in his physician's understanding of his trouble, and in his ability to treat it effectively, little or no progress is likely to be made. It should be explained that dramatic results must not be expected and that reliance should be placed on the judicious application, not of one form of treatment but of a combination of methods which have been carefully thought out. His confidence won, his co-operation secured and the fundamental principles underlying correct treatment observed, a prospect of progressive improvement lies before the patient. Treated early and adequately, the outlook in the severe forms of chronic rheumatic disease is far from being as gloomy as has been formerly held by the laity and the profession. A return to the enjoyment of useful citizenship can be attained in a surprisingly high proportion of cases.

There are three fundamental principles which govern the treatment of all forms of chronic rheumatic disease:—

1. The improvement of the general health of the patient.
2. The elimination or correction of ætiological factors.
3. Treatment of the local manifestation of the disease.

## CLASSIFICATION

It has been thought advisable to adopt as simple a classification as possible, using the nomenclature in common use among general practitioners rather than the more recent terminology based on ætiological concepts over which opinion is still sharply divided. From the point of view of treatment, the chronic rheumatic diseases can be divided into three main groups:—

1. Rheumatoid arthritis.
2. Osteo-arthritis.
3. Non-articular rheumatic diseases.

In a recent paper Osgood has given an excellent definition and comparative classification of the two main groups of chronic rheumatic arthritis, which we quote verbatim:—

“The first, which affects females more often than males, is of more common occurrence in the asthenic individual and has its greatest age incidence in the earlier decades, is called *rheumatoid* arthritis or *atrophic* arthritis or *proliferative* arthritis or *ankylosing* arthritis: ‘Rheumatoid’ because it is not rheumatic fever but presents a somewhat similar articular picture (in the British Isles this is the synonym most commonly employed); ‘Atrophic’ because very early in its course we may appreciate characteristic atrophy (halisteresis) or erosion of bone structure and soon accompanying atrophy of the musculature; ‘Proliferative’ because Nichols and Richardson (1909) showed that an early change, perhaps the very earliest, is a proliferation of the synovial membrane of the affected joints, which becomes thickened (pannus) with the formation of synovial tabs or villi; ‘Ankylosing’ because, in an unchecked disease, the joints may eventually become ankylosed, at first by fibrous adhesions and later by true bony fusion. In this first great type we include Still’s disease in children and, at least for the present, the ‘Marie-Strümpell’ syndrome, or ‘spondylose rhizomélisque,’ the main ankylosing lesions of which usually appear first in the sacro-iliac

joints and spine. The so-called root joints, *i.e.*, the shoulders and hips, frequently are also affected."

There has been much controversy whether rheumatoid arthritis occurs in two forms: (1) the so-called classical or primary type, where a focus of infection is not demonstrable, and (2) the secondary or focal type in which infection is believed to play a definite part. From the point of view of treatment, differentiation between these two forms is unnecessary except in so far as sepsis has to be dealt with in one form and not in the other. In parenthesis, the writers do not wish it to be understood that they agree with the subdivision of arthritis of the rheumatoid type into the two forms mentioned above.

Osgood's definition of group 2 is as follows:—

"The second great type, in which there is no striking difference in sex incidence, although the sthenic body type exhibits it most frequently, and in which subjective symptoms do not usually appear before the age of forty years, is called *osteo-arthritis* (or arthrosis), or *hypertrophic* arthritis, or *degenerative* arthritis, or *non-ankylosing* arthritis: 'Osteo-arthritis' (or arthrosis) (the usual British term) because the bony changes are evident early in the disease; 'Hypertrophic' for the same reason, the articular bone-end changes representing overgrowth or hypertrophy in the form of chondro-osseous spicules or ridges; 'Degenerative' because, as Nichols and Richardson (1909) also demonstrated, the initial changes seem to appear in the articular cartilage in the form of fibrillation and degeneration; 'Non-ankylosing' because neither fibrous nor true bony ankylosis of the joints of the extremities occurs even as an end result of an unchecked disease. One spinal exostosis or spur may fuse with an impinging spur, but the articular bone ends, even after the degenerated cartilage has been completely absorbed, become eburnated (often actually polished), but do not fuse."—"A Survey of Chronic Rheumatic Diseases," pp. 227-278. Oxford University Press, 1938.

We have followed the committee appointed by the British Medical Association in 1933 in excluding from the chronic rheumatic diseases arthritis occurring in the following conditions:—

1. Acute or subacute rheumatic fever.
2. Specific infections: Gonococcal, dysenteric, tuberculous, syphilitic, pyogenic.
3. Metabolic and blood diseases: Gout, hæmophilia.
4. Organic nervous disease: Charcot's joints in tabes and syringomyelia.

The reader is referred to the appropriate sections for the treatment of the primary condition in this group, while the general principles enunciated in the section on chronic rheumatic diseases are in general applicable to the joint manifestations.

## PROPHYLAXIS OF THE CHRONIC RHEUMATIC DISEASES

The importance of diagnosis and treatment in the early stages of disease has been recognized for many years. More recently this principle has been extended to include the preventive aspect of medicine which implies (*a*) the recognition and treatment of individuals whose anatomical and physiological make-up differs in certain respects from the normal, and whom

clinical experience has shown to be peculiarly liable to develop certain diseases, and (b) a study of the effects of external factors in producing disease in normal persons and in those rendered more susceptible by inherent constitutional abnormalities. These principles have been recognized for some time as of fundamental importance in tuberculosis, but in our opinion they are equally applicable to the rheumatic diseases. Accordingly, it appears to us desirable to describe briefly the anatomical and physiological deviations from the normal which occur frequently in individuals who eventually develop chronic rheumatic disease, and also the various external factors of ætiological significance.

Although chronic arthritis does not respect age, sex, social position or anatomic type, clinical experience has shown that (1) a considerable proportion of cases of rheumatoid arthritis are of the asthenic, visceroptotic type, easily fatigued and emotionally unstable; (2) the proportion of females to males is about 3 to 1; (3) the age incidence lies chiefly between puberty and fifty-five years of age; (4) the victims, prior to the onset of arthritis, have often a sluggish deficient peripheral circulation, indicated by their clammy, chilly extremities and inability to tolerate exposure to changes in temperature. In contrast to this group, the majority of sufferers from osteo-arthritis are either of normal build or are of the sthenic, stocky type, with a tendency to obesity and have usually a placid or cheerful outlook. They are often active, energetic people, both mentally and physically. The chief incidence of the disease falls in the latter half of life. It should be pointed out that individuals of the asthenic type are candidates not only for rheumatoid arthritis but for many other forms of chronic disease.

Prophylaxis will be considered under two headings: (1) the improvement of the "soil" by measures directed towards raising the general resistance, and (2) the eradication or reduction of other factors of ætiological importance.

### PROPHYLAXIS OF RHEUMATOID ARTHRITIS

**Measures for Raising General Resistance.**—The general physique can be improved by breathing and postural exercises, details of which will be found in the Appendix. Exercise such as walking, cycling, golfing, etc., in the fresh air should be advised in amounts short of producing fatigue. Should the individual wish to join a gymnastic class organized under the physical fitness campaign, care should be taken that the exercises prescribed are well within his capacity, otherwise more harm than good will result. Attempts to improve the circulation should be made by the use of tepid or warm baths every day, followed by a brisk rub down with a rough towel. Bathing in cold water is generally contraindicated in this class of person. A short annual course of treatment at a spa, if financial circumstances permit, is, we believe, of great value as a preventive measure. Clothing should be light but warm, and the avoidance of wetting and chilling of the feet by the use of suitable footwear is to be recommended. Because of the asthenia and the tendency to become easily fatigued, the family doctor can give useful advice on how to conserve energy, by orderly arrangement of work. For the same reason the doctor should see that adequate rest is obtained, by warning against late hours and by suggesting an hour's rest in the afternoon, if necessary. Mental fatigue is as important as physical fatigue, and

the doctor must play his part by adjusting, by simple psychological means, the minor worries and troubles which beset all of us. Since candidates for rheumatoid arthritis are generally of spare physique below their correct body-weight, common-sense advice regarding the quantitative and qualitative characters of the diet should be given, stress being particularly laid on the value of fruits, vegetables and the dairy products—milk, eggs and cheese. Any tendency towards constipation should be corrected by the measures outlined on p. 561. The anæmia which is so frequently present in women in the pre-arthritic stage should be treated with iron (see p. 470).

By adoption of the régime described, the general resistance will be raised and the liability to infection, believed to be of importance in the ætiology of rheumatoid arthritis, will be lowered. Should, however, any type of infection develop, it should be treated in the asthenic subject with more than the usual care and a longer period of convalescence advised than would be the case in a person of average physique. When focal sepsis is found to be present which the body resistance cannot overcome after being raised as high as possible by the measures outlined above, eradication should not be delayed in view of the known importance of focal sepsis as an ætiological factor in arthritis.

### PROPHYLAXIS OF OSTEO-ARTHRITIS

Osteo-arthritis is more an arthrosis than an arthritis, being a degenerative condition and an accompaniment of the ageing process. It is probable that the most important factor is a constitutional defect in the patient's articular cartilage, which is therefore unable to withstand repeated micro-traumata as satisfactorily as the cartilage of more fortunate individuals. The constitutional factor is analogous to that conditioning the incidence of arteriosclerosis and hypertension. French workers believe that minor congenital abnormalities of the joints are also predisposing factors which are more important than has hitherto been believed. Certain factors, however, can cause or accelerate the process and these may be partly or wholly remediable. They are gross injuries leading to dislocations of joints, fractures of bones which involve the articular surfaces, and excessive or long-continued strains. Accordingly, a short discussion of some of these is appropriate. When a bone is fractured a secondary osteo-arthritis will result in adjacent joints unless proper alignment of the fragments is procured. When a fall or injury occurs, producing trauma of the joint structures and contusion of the overlying tissues, proper treatment by rest followed by heat, massage and movement may delay and minimize the effect of the trauma in conditioning the occurrence of osteo-arthritis. Long-continued trauma from occupational strains is a common cause of osteo-arthritis. It is well recognized that individual trades produce arthritis in particular sites. For example, stone-masons commonly suffer from osteo-arthritis of the wrist, elbow or shoulder, and in agricultural labourers the spine and hips are usually affected. The question arises, when early signs of osteo-arthritis are noted by the doctor, whether a change of occupation should be advised before the affected joints become hopelessly crippled. The decision in such a case will depend on the circumstances, but the advice to change one's occupation in middle age can seldom be taken for economic reasons.

More hopeful fields for the reduction of arthritis and fibrositis in industry lie in the province of public health administration. Improvement of working conditions in factories, workshops, mines, etc., on the following lines would go far to lower the incidence of the rheumatic diseases in industry: (1) the elimination or reduction of exposure to draughts, excessive heat and cold; (2) the provision of rest shelters; (3) the installation of hot baths with the opportunity of changing wet clothes; (4) the adoption of mechanical appliances which would reduce the strain on workers to a minimum by performing weight-lifting operations; (5) the selection of individuals for certain occupations on the basis of physical suitability, and especially the exclusion of people past middle age from occupations throwing excessive strain on the joints.

Another factor which leads to continuous joint strain and undue pressure on the articular surfaces is obesity. Its correction by diet, exercise and endocrine therapy (discussed on p. 383) is a preventive measure of great importance.

Postural defects produce osteo-arthritis for the same reason as does obesity, and their correction by special exercises or orthopædic measures is as important in its prevention as in that of rheumatoid arthritis. The commonest faults are lumbar lordosis and scoliosis, genu varus or valgus, and pes planus.

Focal sepsis is believed to be of much less ætiological importance in osteo-arthritis than in rheumatoid arthritis, but nevertheless, obvious foci should be eradicated when present, as the chronic toxæmia resulting therefrom may be a factor in impairing the general health and thus accelerating the degenerative processes.

## RHEUMATOID ARTHRITIS

The treatment of rheumatoid arthritis is governed by the stage of the disease and the degree of activity present when the patient is first seen by the medical practitioner. We have arbitrarily divided the disease into three stages, although in practice no sharp dividing line exists.

### THE ACUTE STAGE OF RHEUMATOID ARTHRITIS

In order that the objects of treatment may be better understood, a brief description of the main clinical features in the acute stage will be given. Although the joint symptoms are predominant, there is also general systemic disturbance. The patient complains of lassitude even when at rest and of excessive fatigue on the slightest effort. There has been a progressive loss of weight and the appetite is poor. The extremities are cold and clammy, and the body sweat may have a peculiarly rank odour. A moderate fever ranging from 99° to 101° F. may be present. Blood examination shows a moderate degree of hypochromic anæmia, often a slight polymorphonuclear leucocytosis and a marked increase in the sedimentation rate of the red blood corpuscles. Many joints are swollen and painful, the small joints of the hands and feet usually being the first to be affected. The lesions are mainly peri-articular at this stage, only rarefaction of the bone ends being seen on X-ray examination. Muscular wasting is an early and prominent

feature of the disease. The treatment of such a patient embodies two fundamental principles:—

1. General treatment which includes measures (a) to promote the patient's vitality and increase his resistance to infection, and (b) the eradication or correction of ætiological factors.
2. Local treatment of the joints.

**General Treatment.**—The principles applicable to other forms of infection, particularly tuberculosis, are of fundamental importance in rheumatoid arthritis and must be carried out with scrupulous attention to detail if the best results are to be obtained. The importance of treating both the patient and the disease cannot be too strongly emphasized.

As already stated, the *psychological aspect* is of particular importance in all diseases which tend to run a prolonged course. Accordingly the physician must secure the intelligent co-operation of the patient by taking him into his confidence, by explaining in simple language the nature of the disease and the principles on which the treatment to be adopted is founded, and by assuming an optimistic attitude regarding the results to be expected.

Since long-continued fatigue is an extremely important factor in initiating the onset of rheumatoid arthritis or in leading to a relapse, *rest*, both physical and mental, is the first object to be achieved. In the acute stage rest must be complete, and this means that the patient must stay in bed for weeks or even months if necessary until the active phase is past. The desirability of this rest period being undertaken under the best conditions is as important in rheumatoid arthritis as in tuberculosis. Fresh air, sunshine, cheerful surroundings, good nursing and nourishing diet are all factors of importance in improving the physical and psychological state of the patient. Increased institutional accommodation in Great Britain must be an essential feature of any national plan for the control of the rheumatic diseases. It is advisable to explain to the patient that the prescription of rest must be considered as only the first step in an organized scheme of treatment. Recumbency affords the opportunity of correcting faulty posture and, as Goldthwait says, "enables the physician to remodel the body no longer handicapped by the unfavourable influences of gravity." It is of fundamental importance to see that good posture is maintained while the patient is in bed. A firm mattress or fracture boards should be used. Only one firm, low pillow should be allowed at night. A cage should be used to remove the weight of the blankets from the legs and feet. A support for the feet should be provided in the shape of a sandbag or foot-board; and the spine should be kept in good alignment during the day by a back-rest. Lastly, rest in bed enables the nutrition of the patient to be more rapidly improved by dietetic treatment. An important factor in securing rest is the control of pain, which impairs appetite, causes insomnia and increases physical and mental fatigue. For this purpose analgesic drugs must be prescribed in adequate quantities (see p. 810). The practitioner must realize that the analgesic drugs are prescribed solely for the purpose of obtaining rest and thus allowing the other aspects of the therapeutic scheme to be brought into operation, and not because they possess any specific curative properties.

After a week or two of complete rest, when the more active symptoms such as pyrexia may have abated, other measures of value in raising the



general resistance will be employed. A short exposure to *ultra-violet rays*, given on alternate days, acts as a stimulant to the skin and a tonic to the mind. On the other days light *massage (effleurage)* to the body, but excluding the joints, improves the circulation, allays spasm and acts as a general sedative. *The care of the skin* is an important feature in the treatment, because of the defective peripheral circulation and the marked tendency for these patients to sweat a great deal. Accordingly, tepid sponging of the whole body, followed by gentle rubbing with a soft towel, should be carried out at least once a day. Night-wear should be of woollen material, and care should be taken to change the garment as often as required to avoid having damp fabric next the skin. Even at this early stage *exercises* should be prescribed for the purpose of improving the circulation and correcting faulty posture. They are carried out in the recumbent position, and their frequency and amount graduated to suit each individual case in accordance with the degree of asthenia present. Breathing exercises are designed to teach the patient to use his diaphragm and abdominal muscles more efficiently, as by this means the ventilation of the lungs is increased, the oxygenation of the blood improved and the accumulation of blood in the dilated splanchnic vessels mobilized, with concomitant improvement in the general circulation. Postural exercises are given for improving the tone of the spinal and gluteal muscles. We are satisfied, from daily experience of these measures, that the claims made by Goldthwait and Swaim regarding the beneficial effects produced are justified, and we strongly recommend their adoption in every case of rheumatoid arthritis. Details of the exercises for use in the acute stage are given in the Appendix.

**The Removal of Septic Foci.**—Since it is generally agreed that an infective factor is of particular importance in rheumatoid arthritis, the problem of focal sepsis requires careful consideration. In some cases the history and clinical manifestations show that an infection has occurred of such virulence as to warrant the deduction that it is the prime ætiological factor. In many cases, however, the evidences of infection are more uncertain, and in others the most careful clinical investigation leads to negative results. It is possible, however, that in the last group infection may have played a part, although evidence of its occurrence can no longer be found or alternatively it may be present but cannot be located by available methods of investigation. Accordingly it has been argued that the response of the body to infection is frequently of equal importance in causing the disease as the infection itself. Accordingly, it is not surprising that the results obtained by the eradication of focal sepsis are frequently unsatisfactory if it constitutes the only therapeutic procedure. If a focus of infection exists which is not removed, it may seriously mitigate the chances of recovery, even when all other forms of treatment have been applied. The discovery of focal infection and the assessment of its ætiological importance may offer the greatest difficulties, since it is recognized that focal sepsis may occur as the result of the lowered vitality of the individual, consequent on the disease. It follows from this that when doubt exists, a conservative policy should be adopted until sufficient time has elapsed to evaluate the effects of the measures for raising general resistance. If improvement occurs, conservative treatment should be continued until its maximum effects have been obtained, and the patient's condition is such that eradication of the focus will entail the least danger of precipitating a relapse, should the focus still

show signs of activity. If, on the other hand, no benefit accrues from conservative treatment, it is possible that the focus of infection is responsible for the continued activity of the disease, and its removal should be undertaken. It is desirable, before advising operation, to discuss with the patient in simple language the problem of focal sepsis as outlined above and the reasons which favour operative interference in his particular case. The patient should be told that removal of the focus by itself may not cure his arthritis but constitutes only a part of the plan of treatment for the reduction of toxæmia and the raising of his resistance. Before the removal of teeth or tonsils we routinely give 1 gramme of sulphathiazole or sulphadiazine or 30,000 units of penicillin four-hourly for the day preceding and following the operation with the object of inhibiting the temporary bacteræmic state which may follow such interference.

Septic foci are of two types, those which are easily accessible for investigation, *e.g.*, teeth, tonsils, etc., and those which are not, *e.g.*, gall-bladder, appendix, etc. We do not intend to describe the symptoms and signs on which the diagnosis of infection in any individual organ is made, or to give in detail the methods of treatment required, but will merely enumerate in order of importance the sites in which foci of infection in rheumatoid arthritis are likely to occur:—

1. First in frequency and importance is tonsillar sepsis. The younger the individual the more frequently will this be found.

2. Dental sepsis. In our experience apical abscesses are more important as sources of infection than pyorrhœa alveolaris. In the more elderly patients dental sepsis is as important as tonsillar sepsis.

3. The accessory air sinuses, particularly the maxillary antrum.

4. Sepsis of the urogenital tract. In males, where no obvious sepsis of the mouth or throat can be found, the prostate should always be palpated and its secretion examined under the microscope for organisms and pus cells. Gonococci are seldom demonstrated in the smears, the original invasion having been succeeded by a low-grade infection, usually streptococcal or staphylococcal in origin. The latter organisms are held by some authorities to be primary infective agents in many cases. If prostatitis is present, drainage of the organ must be assisted by prostatic massage, which at first must be done very gently and gradually increased in vigour, otherwise severe local pain and constitutional disturbances may result. In women, pelvic sepsis, with the exception of chronic salpingitis, is not of the same ætiological importance as it is in men. We have had under our care cases of rheumatoid arthritis with multiple and widespread lesions which failed to respond to all forms of treatment until tubal infection was discovered and eradicated. Some physicians, however, believe that chronic cervicitis is an important focus of infection in rheumatoid arthritis and claim excellent results from the use of pelvic diathermy. We believe that these claims have been exaggerated.

5. Chronic cholecystitis and appendicitis are uncommon sources of focal infection. In view of the deleterious effects which major operations may have on severely debilitated individuals, unequivocal signs of infection must be present before laparotomy is advised.

Since the family doctor cannot be expected to have specialized knowledge of all the organs of the body, the need for team work is obvious in the

investigation of a case of rheumatoid arthritis, and the physician in charge of the patient should have at his disposal the services of a laryngologist, dentist, radiologist, etc.

In conclusion, we would again stress the difficulty of recognizing and assessing the importance of septic foci and the need for wide experience and sound judgment in deciding what measures should be adopted in each individual case.

**Drugs.**—Of the hundreds of remedies used in the treatment of the chronic rheumatic diseases, the majority are useless. Some may be harmful and only a few are of proved value. It is best for the physician to realize that no drug has been shown to have a specific curative action in rheumatoid arthritis. Used intelligently, however, drugs can make a useful contribution to treatment. For this purpose the analgesic, sedative and hypnotic drugs are of particular value since pain, nervousness and insomnia are potent factors in hindering recovery. Aspirin, 10 gr. (0.6 gm.), phenacetin, 5 gr. (0.3 gm.), codein,  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (15 to 30 mg.), phenazone, 5 to 10 gr. (0.3 to 0.6 gm.), chloral hydrate, 15 gr. (0.9 gm.), and the barbiturates, singly and in various combinations, are frequently employed. The injection of morphia or heroin is contraindicated because of the danger of habit formation. If anæmia is present, iron is indicated. Liver extract by mouth or by injection is useless and expensive and should be employed only if megaloblastic anæmia co-exists, which is very rarely the case. Calcium is not required if the patient is drinking plenty of milk. Provided the diet is well balanced and adequate in amount, it is doubtful if supplements of vitamins are really of value (see p. 394). The claims made in America in regard to the favourable effects of large doses of vitamin D (100,000 to 300,000 units daily) in influencing the course of rheumatoid arthritis have not been confirmed. Endocrine preparations should not be prescribed unless clinical evidence of a state of glandular deficiency is present. Cincophen and colchicine are contraindicated, because the metabolism of uric acid is not deranged in rheumatoid arthritis. Recently prostigmine has been used in rheumatoid arthritis for the relief of muscular spasm. The initial claims have not been substantiated by other workers. The physiological basis for the use of the drug for this purpose appears to be unsound, and in the doses advocated the effects of parasympathetic stimulation are very unpleasant. These can be mitigated by the simultaneous administration of atropine. The use of prostigmine is not recommended. In view of the alleged ætiological importance of hæmolytic streptococci in rheumatoid arthritis it was hoped that penicillin and the sulphonamide drugs would be of particular value. Clinical trial has, however, revealed no beneficial effects from their exhibition. This is not surprising if the arthritis is the result of sensitization and not of infection of the joints. Mention must be made of the Swedish drug salazopyrin, which is a combination of sulphapyridine and aspirin and which has been claimed to be of value if given daily over periods extending to a year or longer. These claims must await further independent investigation before being accepted. It is, however, of interest to remember the undoubted value of a small daily dose of sulphonamide in preventing relapse in patients who have had rheumatic fever, and an open mind must be kept as to whether similar long-continued treatment might not influence the course of rheumatoid arthritis.

Of the multitude of drugs and remedies used empirically, mention must

be made of arsenic, iodine, sulphur, guaiacol, orthiodoxybenzoic acid, histamine, bee venom and the thiosinamine group of drugs. Claims in regard to their value are largely based on clinical impressions and not on controlled research. Their use is sanctified by tradition rather than by factual evidence of their efficacy, and the mechanisms by which they are alleged to act are uncertain. In the present state of our ignorance, the physician is entitled to prescribe any of these preparations if he so desires provided he realizes that they have no specific curative properties and are no substitute for a carefully thought-out plan of treatment on the lines described in this chapter.

*Chrysotherapy.*—It is widely agreed that the introduction of gold salts constituted an important advance in the treatment of rheumatoid arthritis. It should be clearly recognized that the exhibition of gold salts must be considered merely a part of and not a substitute for a general plan of treatment carefully arranged for each particular patient. Chrysotherapy can be employed at any stage of the disease provided the process is still active as indicated by the clinical state and the presence of a raised blood sedimentation rate. The oil-soluble and water-soluble salts are equally effective provided the dosage of gold is the same. Since the water-soluble preparations are cleaner and easier to handle, they are to be preferred. Myocrisin, a 50 per cent. solution of sodium aurothiomalate in water, is a proprietary preparation widely employed. Preparations of colloidal gold are not recommended. The mode of action of gold in rheumatoid arthritis is unknown. Some authorities believe its beneficial effects are due to its bacteriostatic properties, while others hold that it stimulates the reticulo-endothelial system or alters the immunological mechanism in some way as yet unknown. Following the injection of gold salts, the level of gold in the plasma rapidly rises and gold is thereafter deposited in every cell in the body. The highest concentration is found in the liver, kidneys and skin, sites which clinical experience has shown to be chiefly affected by toxic reactions. Another point of clinical interest is that gold is present in the synovial membrane in much higher concentration than in muscle and that the gold content of the synovial membranes of joints the seat of arthritis is much bigger than in the synovial membranes of normal joints. Excretion is largely by the kidneys, but a marked retention occurs in the body when the usual weekly dose of 100 mg. (0.1 gm.) of gold salt is given. At least 80 per cent. is retained in the body and consequently the excretion of gold can be demonstrated in the urine for many months after treatment has ceased.

The above information is of great clinical interest as it explains some of the dangers of chrysotherapy and why certain organs are especially affected by toxic reactions. The desirability of giving smaller doses over longer periods than is usually practised is also rendered intelligible. By this means toxic reactions can be reduced in frequency and severity and the number of patients who will be enabled to continue treatment will be increased. The course of chrysotherapy generally recommended at the present time consists of twelve injections at weekly intervals, the first three containing 0.01, 0.025 and 0.05 gm. and the last nine of 0.1 gm. of gold salt, making a total of approximately 1 gm. In the future it may be shown that better results are obtained by giving the same amount over a period of six months and limiting the quantity injected at one time to a maximum of 50 mg. (0.05 gm.) of gold salt. When the course has been completed, no further injections of gold should be given for eight weeks. Thereafter

the course should be repeated for a second, third or fourth time, depending on the clinical response and the absence of reactions.

Toxic reactions have been reported as occurring in from 20 per cent. to 50 per cent. of patients undergoing chrysotherapy. In approximately 5 per cent. the reactions are severe and serious. A fatality rate of 1 per cent. has been reported. There is no satisfactory method of preventing their onset and no way of recognizing which patients are susceptible to gold. Hence it is advisable for the physician to explain the dangers to the patient or his relatives before beginning treatment, at the same time pointing out that the therapeutic advantages expected outweigh the risks. Gold treatment should not be recommended if serious organic disease is present, particularly if it affects the liver, kidneys, hæmatopoietic tissues or skin. Before each weekly injection, careful questioning and clinical examinations including testing the urine for albumen and, ideally, leucocyte counts should be undertaken to elicit the earliest signs of damage to these organs and tissues. Recent work suggests that the value of routine leucocyte counts has been exaggerated since agranulocytosis may appear abruptly within two or three days of the count being found normal. In many clinics, when leucotoxic drugs (gold, arsenic, thiouracil) are used, routine white cell counts have been abandoned in favour of careful instructions to the patients to report to their doctor immediately any symptoms of general ill-health, fever, or sore throat develop. General skin reactions, purpura, marked leucopenia, jaundice, albumen, casts and blood in the urine are findings of grave significance and are indications for complete cessation of gold treatment. Mild stomatitis and gastro-intestinal disturbance, slight leucopenia and itchiness of the skin are danger signals which warrant temporary cessation of treatment. Gold salts should not be given again until all symptoms and signs have disappeared, and then to begin with only in reduced dosage. A recurrence of toxic signs is an indication for a permanent discontinuation of chrysotherapy. A trace of albumen in the urine by itself is not a contra-indication to continued treatment but indicates the need for careful urine analysis prior to each subsequent dose of gold. With the reduced amounts of gold advised above, it is believed that less than 10 per cent. of patients will have to discontinue treatment because of toxic reactions, while 80 per cent. will derive benefit both to the general health and to the local arthritic manifestations. Reference should be made to the appropriate sections for the treatment of the various toxic manifestations should they arise. Until recently treatment has been purely symptomatic. The drug B.A.L. (British anti-Lewisite), originally designed for the treatment of arsenical poisoning, has been used with gratifying results for the treatment of various toxic manifestations arising from gold therapy. The drug combines with most heavy metals to form a stable compound which is rapidly excreted in the urine. For all forms of severe toxic reaction, B.A.L. is given in doses of 3 mg. per kilogram body-weight every six hours for 3 to 4 days. The calculated quantity is injected intramuscularly. Smaller doses will be found effective for less severe toxic reactions. In gold hepatitis the dose should never exceed 3 mg. per kilogram body-weight given at six-hourly intervals and should generally be less since it has been shown that in cases with liver damage the toxic effects from B.A.L. may be severe. The drug is marketed by Boots Ltd. in 2-c.c. ampoules each containing 100 mg. in solution in oil.

**Vaccines.**—While it is universally accepted that vaccines can produce valuable effects in the prevention of certain diseases due to known infective agents, it is highly debatable whether they are of any value as curative agents in established disease. It is, therefore, not surprising that considerable scepticism exists in regard to their therapeutic value in rheumatoid arthritis, a disease whose aetiology is unknown and which may not be due to a bacterial infection at all. Nevertheless, vaccine treatment must appeal to those who believe that the pathological changes in rheumatoid arthritis are sensitization reactions to bacterial antigens absorbed from foci of infection. It might be thought that since many thousands of cases of rheumatoid arthritis have been treated with vaccines during the past twenty-five years indisputable proof of their efficacy would have been produced by those who advocate their employment. Unfortunately this is not the case. Reiterated claims that clinical benefit is produced in a certain proportion of cases are no substitute for statistical data obtained from a properly controlled experiment which should demonstrate a significantly higher proportion of good results in cases treated with vaccines compared with a control series receiving injections of sterile saline. Without such information it is impossible to know whether the clinical results obtained can be ascribed to the vaccine used or to the improvement which occurs in approximately 50 per cent. of cases without any specific treatment, augmented by the psychological effects of parenteral injections or the personality and enthusiasm of the physician in charge of the case. The need for properly controlled research in this field is urgent. While the therapeutic value of vaccines is at least debatable, it is universally agreed they are potentially dangerous if employed injudiciously in the acute stage of the disease or in excessive doses. Gross deterioration in the general health and local arthritic manifestations will certainly result if vaccines are given in amounts which produce marked general reactions. At the time of writing the majority of physicians believe that vaccines are of doubtful value and accordingly their employment is not recommended routinely. If they are to be used, they should be reserved for cases which have failed to show satisfactory progress on the general plan of treatment as outlined above and for patients for whom gold is contra-indicated.

It is a matter of personal opinion whether stock vaccines or autogenous vaccines made from organisms isolated from a septic focus believed to have been of aetiological significance should be employed. It is generally agreed that a vaccine should be given over a prolonged period, in small doses, with the careful avoidance of significant reactions. The production of a constitutional disturbance may have a serious deleterious effect on the patient's health and on the local manifestations of the disease in the joints. This is particularly liable to occur in the active stage of the disease when fever is present. Accordingly, we feel that vaccine therapy is contra-indicated except in the subacute or chronic stages. Although some authorities claim that the best results are obtained from the intravenous injections of vaccines, this is disputed by others, and since the technical difficulties are greater and the chances of serious reactions higher, we advise the practitioner to continue using the subcutaneous route. The intervals between injections should be about a week and the initial dose should be sufficiently small to ensure that no general reaction results. Usually, an amount of vaccine containing approximately one million organisms

will fulfil this requirement. Some authorities believe that even a smaller initial dose is indicated. For subsequent injections, the dose is gradually increased until a feeling of slight malaise or an increase of pain in the joints occurs. This reaction is usually accompanied by a small rise in temperature, the recognition of which is of importance in assessing the subsequent dose of vaccines. It is advisable, therefore, to take temperature readings night and morning, or better still, at four-hourly intervals during the twenty-four hours after the injection. Even a mild reaction is an indication that the dose of vaccine should not be increased at the next injection. Should a similar reaction occur with the same dose, a decrease to the amount which fails to provoke a reaction is indicated, and this dose should be continued as long as improvement is occurring. Should no benefit accrue within from two to three months of the institution of the course, injections should be stopped. On the day of injection and for twenty-four hours thereafter, all forms of active physiotherapy should be withheld, since they tend to increase the reaction to the parenteral administration of foreign protein. The one undoubted benefit which the weekly injection of any substance including vaccines has to offer is that it enables the physician to see his patient at regular intervals and gives him the opportunity of reviewing the progress of the case and of making adjustments to the therapeutic programme when necessary. In addition, parenteral treatment appears to have a more beneficial psychological effect on patients in general than peroral treatment, and anything which helps the patient to keep up his courage is of value in all forms of chronic debilitating disease.

**Non-specific Protein and Fever Therapy.**—These forms of treatment are employed much less frequently to-day than fifteen years ago, thus indicating that the original claims regarding their therapeutic action were undoubtedly exaggerated. Both the parenteral injection of foreign protein and the raising of the body temperature by the use of hot baths and packs, hot-air cabinets or short-wave machines produce an increase of blood flow, changes in the permeability of cell membranes, heightened metabolism, leucocytosis and a stimulation of antibody production. The degree of the reactions produced depends on several factors, the chief of which are the type and amount of material introduced, the route used for injection, the duration and degree of the temperature induced and, lastly, the individual variation in response of the patient. Whichever method is employed, a reduction of pain, stiffness and swelling may be expected to occur in a proportion of patients, but unfortunately these beneficial results are of temporary duration. In a small minority of cases the effects may be both dramatic and sustained. The methods employed may be relatively simple, safe and suitable for use by the general practitioner, or complicated and dangerous, when they should be used only in hospitals and nursing homes and by experienced physicians. Of the former, mention may be made of hot baths at a temperature of 100° to 105° F. for twenty minutes and the intramuscular injection of peptone solution, boiled milk (5 c.c.), xifal milk (2 c.c.), colloidal sulphur (2 c.c.) and Pyrolactin D (2 c.c.), a proprietary preparation containing milk and sulphur. A series of injections are given at 5 to 7 days' intervals, the dosage being progressively increased according to the patient's response. The intravenous injection of T.A.B. vaccine produces much more severe reactions. The initial dose is 25 to 50 million organisms, the quantity being doubled at each subsequent injection, due consideration



being given to the effects produced. The course should rarely exceed six injections.

Certain of the observations on vaccine therapy given in the previous section are equally applicable to non-specific protein and fever therapy; namely—the beneficial effects do not occur sufficiently regularly to suggest the employment of these forms of treatment in all cases of rheumatoid arthritis. They should be reserved for subacute and chronic cases when the general lines of treatment, including gold salts, have been applied and a stage has been reached when stiffness and limitation of movement are the presenting symptoms and further progress is not being made or where toxic reactions to gold have developed. Non-specific fever treatment is contraindicated in the acute pyrexial stage of the disease. Only the milder methods should be employed in the subacute and chronic stage if the patient is underweight and in a poor state of health, otherwise a marked deterioration in the general and local manifestations of the disease may result.

**Diet.**—The diet should be well balanced and should contain sufficient calories to restore the body-weight to normal in patients underweight, while for obese patients it should be subcaloric. Small frequent meals attractively served will help to stimulate appetite. There are no contraindications to any particular article of diet and there is no sound reason for believing either that nutritional deficiency is the cause of rheumatoid arthritis or that any food factor has any specific curative value. The need for an adequate intake of protein and an ample supply of vitamins and minerals is based on the general physiological principles which govern the dietetic requirement of a patient suffering from a chronic wasting disease in which metabolism may be further increased by fever. A liberal fat allowance should be prescribed in the shape of milk (up to 2 pints daily), cream, eggs and bacon. By this means the required intake of first-class protein, phosphorus and calcium will also be assured. An average helping of meat or chicken at one meal and a fish or egg dish at another should be allowed. Ample fresh fruit and vegetables are indicated. In the acute stage when digestion and appetite are impaired these should be served in the form of juices, jellies and purées and the amount of starchy food such as bread and potatoes may require to be limited. It is usual to prescribe additional vitamins (A, B, C and D) although it is doubtful if this is necessary when the diet has been properly constructed. Cod-liver oil or one of its concentrates such as liq. vitamin A et D conc. (B.P.) is believed to be of special value by certain authorities.

**Gastro-intestinal Tract.**—It has long been recognized that patients with rheumatoid arthritis have a poor appetite and frequently suffer from digestive disorders. Since radiographic studies indicate a general hypotonia of the stomach and intestines, the latter showing elongation, dilatation and ptosis, with markedly reduced haustration, it is not surprising that stasis of the intestinal contents is present. Accordingly, the supporters of the theory of auto-intoxication hold that the bowel must be considered as an important site of focal sepsis in rheumatoid arthritis. We feel, however, that the gastro-intestinal abnormalities are more likely to be the result rather than the cause of the disease. Such a view does not imply, however, that their treatment should be neglected. For this purpose dietetic measures are of particular importance, for it has been shown by Fletcher of Toronto that in



such cases it is possible to restore partially or entirely the normal tone of the bowel.

The dietetic treatment of rheumatoid arthritis has already been described. Additional measures are the avoidance of purgatives and the use of liquid paraffin in small doses two or three times a day, supplemented, if necessary, by mild laxatives such as salines, senna or cascara. Postural and breathing exercises (see p. 844) and abdominal massage are also helpful. Colonic lavage does not appear to us to be a physiological method of treating constipation. If used at all it should be given on alternate days on three or four occasions, with the object of emptying a heavily laden colon, as a preliminary to the institution of the régime already described. For further details regarding the treatment of constipation see p. 561.

Intestinal antiseptics, such as salol or guaiacol, are frequently prescribed, and sulphur has also been recommended, both because of its supposed intestinal antiseptic qualities and because of the somewhat doubtful evidence of its abnormal metabolism in rheumatoid arthritis. There is little scientific evidence to justify their use.

**Endocrine Glands.**—We know of no satisfactory evidence to prove any direct relationship between chronic arthritis and disorders of the endocrine glands. It is true that arthritis may occur in a proportion of patients at the menopause, and in some cases of myxœdema, gigantism and acromegaly, but the joint changes can best be explained on the basis of mechanical strain and trauma resulting from obesity, skeletal changes and faulty posture. Thyroid extract and œstrogenic preparations should be prescribed in cases of arthritis only if the appropriate symptoms of glandular deficiency are present.

**Local Treatment.**—During the acute stage of rheumatoid arthritis the affected joints are swollen and exquisitely tender. The slightest movement is accompanied by severe pain and the muscles moving the joints are continuously in spasm. The patient soon discovers the position of greatest ease for the throbbing joints, and is often aided by sympathetic relatives, who little realize that by placing the joints in the flexed positions of the patient's choice they are preparing the way for the establishment of the dreadful deformities which are only too commonly the permanent legacy of rheumatoid arthritis. Such a patient lies with flexed knees, flexed hips, flexed elbows. The forearms and hands are laid on the chest, the wrists in a position of palmar flexion, and the feet are allowed to remain plantar flexed for lengthy periods. As the disease progresses, peri-articular and intra-articular adhesions form and movement becomes progressively more limited.

There are two fundamental principles underlying local treatment during the active stage of the disease. The first is the prevention of deformity and the second is the maintenance of function. The spasm of the surrounding muscles is Nature's attempt to immobilize the inflamed joints and is largely responsible for the wasting which is such a prominent feature of the disease. As a result of the long-maintained position of flexion, the flexor groups of muscles undergo compensatory shortening and thus still further limit the range of movements. Pain, therefore, must be relieved at all costs. It has already been emphasized that analgesics in adequate dosage are essential, but this alone will not suffice. The affected joints must be completely immobilized in order to avoid stretching of the inflamed structures,

and this is most satisfactorily obtained by application of properly fitting splints. The relief obtained by fixation in such splints is of great therapeutic value, as it allows the patient to sleep without the large doses of sedatives previously required, with consequent improvement in the mental outlook. The muscles, relieved of their burden by the splint, relax, and wasting is reduced to a minimum. Thus, the fundamental principle of rest must be applied locally to each affected joint if the patient is to enjoy the mental and physical relaxation so essential to his well-being.

Light, easily removable, perfectly fitting splints can be made quickly and simply with muslin bandages impregnated with plaster of Paris. The technical details for their manufacture are given in the Appendix. Whenever possible the splints should be skin-tight, as this ensures complete immobilization of the joints, since the slightest movement within the splint will induce the return of pain and spasm. In very thin patients it may be necessary to pad the bony prominences. This is best done by means of small pieces of chiropodist's felt, which are easily cut to shape and adhere to the skin. Before applying the plaster the skin should be oiled or the limb encased in stockinet, which forms an effective lining to the splint. Since in some of the more severe cases ankylosis may take place in spite of treatment, the splint should hold the joint in the position which will produce the best functional result, should this occur. For example, the wrist should be put up in slight dorsiflexion, the foot midway between dorsi and plantar flexion.

Although we believe that splints made by the plaster technique are ideal, their application requires some degree of technical skill, and other materials may be found more convenient. Aluminium can readily be cut and shaped to form a splint for any joint, and can be purchased in sheets of the correct thickness for this purpose. Poroplast when soaked in hot water becomes pliable and can be moulded to any shape required. When dry it forms a light and rigid splint. It has been claimed that prostigmine reduces muscular spasm and should therefore be given in full doses before the application of splints. We do not accept this claim for reasons given on p. 810.

The use of properly fitting splints is a most important advance in the treatment of the joints in rheumatoid arthritis. By this means swelling is reduced more quickly and pain relieved more effectively than by any other method. Whatever material is used, the splint should be easily removable in order that the second principle underlying treatment may be observed. Function is maintained in the inflamed joints during the acute phase of the disease by movement. Active movement by the patient is preferable to passive movement by the masseuse. The splints are removed once daily and each affected joint is gently moved. The movements should be well within the patient's limit of tolerance, and an increase in pain or stiffness which lasts more than an hour or two is an indication that this has been exceeded. A single movement daily is sufficient to prevent the occurrence of ankylosis. Any effort to force the inflamed joints through their full range of movement will result in increased disability. A full dose of an analgesic, such as aspirin, phenacetin and codein given 1 to 2 hours previously, will reduce pain to a minimum. Movement should be preceded by heat in some form, because of its effect in diminishing pain and spasm and improving the local circulation. The particular form of heat employed is not of great importance, provided that the joints are thoroughly warmed. Radiant heat, or infra-red lamps which are portable and can be plugged

into any lighting circuit, are admirable sources of heat for this purpose. Moist heat, in the form of mud packs, peat packs or cataplasma kaolin, are also of great value as a preliminary to movement. Perhaps one of the best methods of applying local heat is by means of paraffin wax baths. Full details regarding the use of mud and wax are given in the Appendix. The nutrition and tone of the muscles are maintained by light massage (*effleurage*), but the joints themselves are avoided as no useful purpose, but rather the reverse, is served by massage applied over a swollen and inflamed joint. The patient must also be taught to contract the muscles without moving the joints (static contraction), since voluntary contraction is the physiological method of maintaining the health of muscles. In the early stages, especially when marked wasting is present, faradic stimulation may be necessary, but should be replaced by active contractions as soon as possible. As the activity of the disease begins to subside and the patient's general condition starts to improve, active movements of the joints are instituted, assisted at first in order to throw a minimum strain on the articular structures. Later, simple exercises are prescribed (see Appendix), but weight-bearing must be avoided until the active phase of the disease has passed.

The more active forms of local treatment are not applicable during this phase of the disease, when they do more harm than good. They will be fully discussed in the treatment of subacute and chronic stages.

### SUBACUTE STAGE OF RHEUMATOID ARTHRITIS

The patient may reach the subacute stage after weeks or months of treatment in the acute stage. Alternatively the disease may commence insidiously and the patient presents himself for treatment in the subacute stage. Characteristically one or more of the joints is swollen and painful, a considerable degree of asthenia and muscular wasting is generally present, fever is absent, but the sedimentation rate is raised to a figure of 30 to 50 mm. in one hour. In such cases the investigations described and the measures advised for the raising of the general resistance and the eradication of factors of aetiological importance must be undertaken with the same attention to detail as in the acute stage. This includes the search for septic foci and their eradication, the provision of adequate mental and physical rest, attention to the gastro-intestinal tract, the prescription of a nourishing diet, the instruction of the patient in breathing and postural exercises, the administration of drugs, including the gold salts, and the application of local measures for the relief of pain, prevention of deformity and maintenance of function. In cases which have passed into the subacute from the acute stage, the transition from recumbency to active movements and weight-bearing must be made gradually.

It is essential to bear in mind the fact that rheumatoid arthritis is a general disease, and that even if the weight-bearing joints are not or only slightly involved, this in no way invalidates the need for general bodily rest for considerable periods in the day in order to counteract the general fatigue invariably present. The failure to obtain adequate rest in women of the working classes treated at home is an important factor in mitigating against the production of good results from treatment of these cases. The benefit derived from resting the swollen and painful joints in splints is

as great in the subacute stage as in the acute, but the number of hours per day during which the joints are immobilized should be reduced according to the degree of activity still present. Thus, in some cases, splints fitted to the wrists may be worn only at night, while in more active cases they may have to remain in position throughout the day except at meals.

In the subacute stage physiotherapy plays a more important part in the treatment than it does in the acute stage. The measures for the application of heat locally, *e.g.*, radiant heat, wax baths, mud packs, etc., are as useful in this stage as they are in the acute. In addition, hydrotherapy may be extremely valuable as a means of improving the function of the skin as well as for its effect of causing absorption of effusions and helping to restore movements to stiff joints. Accordingly, it is only in the subacute and chronic stages of the disease that it is advisable to send patients to spas for treatment, and this should be done before irreparable structural damage to joints has occurred if the best results are to be obtained. *Ætiological* factors such as focal sepsis should be corrected first. The family doctor in making his selection of the spa should be guided by certain considerations, such as the weather which may be expected at the time of his patient's visit, the type of treatment desired and the general amenities available. For elderly, feeble patients there is an obvious advantage in choosing the spa nearest the patient's home, while in other cases the further the patient is removed from the influence of home and relatives the better. A reliable guide for the choice of a spa is now available to the medical profession in the official handbook of the British Health Resorts Association. A full report of the patient should be sent by the family doctor to the spa physician. The main cost of spa treatment is that of board and lodging, which may vary from three guineas a week upwards, depending on whether the patient is in a boarding-house or in a luxury hotel, while the cost of actual treatment averages about a guinea a week. The average duration of a "cure" is about three weeks.

**Physiotherapy.**—We have already discussed the part played by hydrology as a preventive measure in the frigi-sensitive individuals who are peculiarly liable to develop the chronic rheumatic diseases, in re-educating the skin to respond more normally to the effect of cold and damp. Hydrology also plays an important part in the treatment of chronic rheumatism. The use of hyperthermal waters is of particular value.

In a hot bath pain is relieved and muscular spasm is largely eliminated. Non-weight-bearing movement is facilitated, and the rise in body temperature acts as a general stimulus to metabolism. Three types of bath are in general use—the deep bath with undercurrent douche, the subaqueous massage douche, and the hot pool.

In the deep bath the patient can stand or sit in water at a temperature of from 95° to 100° F. The bath is of a sufficient size to allow of free movement of all the joints and of sufficient depth to reduce the action of gravity to a minimum. Controlled percussive massage is applied by an undercurrent douche of water ejected from a 2-in. hose-pipe at a temperature 5° to 10° hotter than the bath (subaqueous massage). The massage douche may be of the Vichy type, where general massage of the muscles is given to the patient lying in a shallow trough under a fine spray of hot water. Finally, each joint is put through its possible range of movement without the use of force. As previously stated, active movements by the patient are prefer-

able to passive movements by the masseuse. In the Aix type of massage douche the patient may be sitting on a stool or reclining on a table. General massage is given, while a jet of hot water, emerging from a hose carried over the operator's shoulder, is played on the part being treated. The usual temperature of the water used is 100° to 105° F., and the treatment lasts for twenty minutes. The hot pool is a small swimming bath with parallel bars running across it to enable the patients to support themselves while taking exercise. Undercurrent douches may also be provided. Patients who are unable to walk may be lowered into the bath on a canvas stretcher or a chair operated from a gantry. The hot pool bath is of particular value in enabling the patient to move his joints actively without weight-bearing.

Following any form of hydrotherapy it is important that the patient should be placed in hot wraps in order to achieve free sweating and to maintain it for fifteen to twenty minutes after the bath. The patient should then be allowed to cool down slowly in a warm room, at least one hour's rest being prescribed. Immersion baths cause considerable exhaustion to debilitated patients. They should not exceed fifteen minutes in duration, and in general should not be given more than three times in a week. Particular care must be observed in prescribing immersion baths in cases of rheumatoid arthritis, as more harm than good may result if excessive fatigue is produced. (There is real need for issuing a warning regarding the dangers of overtreatment in asthenic individuals suffering from arthritis.) On alternate days the joints should be treated by local applications of heat in the form of mud packs, wax baths, kaolin poultices, radiant heat, etc.

Electrical treatment may also be of service, and the continuous or galvanic current, diathermy and short-wave treatment are valuable for their sedative effect. The interrupted current (Faradism) is used to improve the condition of wasted muscles in the neighbourhood of arthritis joints. As soon as the patient can adequately contract the affected muscles, Faradism should be replaced by active exercises carried out for short periods twice or thrice daily. Ionization with sodium salicylate, potassium iodide or histamine is claimed to be of value in relieving pain and dispersing effusions. Since the drugs are removed almost immediately from the site of ionization via the underlying capillaries, it is difficult to understand the rationale of this treatment except as a form of mild counter-irritation.

Massage plays an important part in the treatment of all rheumatic diseases. When properly applied, massage improves venous and lymphatic drainage, promotes the removal of peri-articular effusion and produces muscular relaxation. It should be applied to the muscles surrounding the joints. If massage is to be applied to the joints the disease process must be quiescent, and it should be of the light stroking type (*effleurage*).

Active movement and re-educational exercises are of the greatest value in the restoration of function. In the subacute stage movement of the joints under water is particularly beneficial. Re-educational exercises, under the guidance of a properly trained technician and devised according to the individual patient's needs, play an important part in the prevention and correction of deformity and the restoration of function.

Much can be done at home for those who, for financial or other reasons, are unable to visit a spa. The various methods for the production of local heat already described are available everywhere, and electrical treat-

ment can be given in all general hospitals and modern nursing homes. Hydrotherapy may be provided in the patient's home by using the household bath, which should be filled with 30 to 40 gallons of water at a temperature of 98° to 105° F. The addition of 3 to 6 lb. of common salt will make a brine bath with a saline content equivalent to that of sea water. Epsom salts (1 to 2 lb.) or washing soda ( $\frac{1}{2}$  to 1 lb.) can also be used. A mustard bath is another excellent means of raising body temperature and causing a rubefacient effect. Half an ounce of mustard is made into a smooth paste with cold water before being added to the bath. This method is contraindicated in the presence of any skin disease and should not be used in patients with rheumatoid arthritis and psoriasis. The patient is completely immersed in the bath for a period of from five to fifteen minutes, depending on the general condition. Thereafter he should be well wrapped in hot towels and remain in bed for at least an hour. For more debilitated persons partial immersion baths should be employed since they are much less exhausting. The patient sits in a hip bath half filled with water at 100° F., with his feet in a foot bath containing water at a temperature of 100° to 105° F. The duration of the bath should be from ten to twenty minutes, and it should be followed by a similar rest period as already described. Complete or partial immersion baths should not be given on more than three days a week.

**Drugs.**—In addition to those mentioned in the section devoted to the acute stage, bee venom, histamine and the thiosinamine groups of drugs (fibrolysin, iodolysin) have been recommended in the subacute and chronic stages of rheumatoid arthritis. We have little doubt that the claims made on behalf of such preparations have been exaggerated. We do not use them ourselves and we believe that the views expressed on p. 810 on drugs used empirically are equally applicable here.

### CHRONIC STAGE OF RHEUMATOID ARTHRITIS

If all cases of rheumatoid arthritis were correctly treated in the acute and subacute stages deformities would be met with much less frequently. However, much can now be done to improve the lot of those patients in whom the active phase of the disease has passed but in whom marked deformities have arisen in the joints.

In addition to the physiotherapeutic methods already described, special procedures are required for the correction of deformities and restoration of function, which are wholly orthopædic in nature and may include surgical intervention in a small proportion of cases (see *Surgery in Arthritis*, p. 837).

**Correction of Deformities.**—The commonest deformities are fixed flexion of the hips, knees and elbows, limitation of abduction and rotation in the shoulders, limitation of movement or ankylosis of the wrists in palmar flexion and of the ankles in plantar flexion, subluxation of the metacarpophalangeal joints with ulnar deviation of the fingers, subluxation of the interphalangeal joints, flat foot and hallux valgus. The joints usually become fixed in the position which is most comfortable to the patient during the acute stage, as has been previously mentioned. The maintenance of the joints in these positions for long periods leads to the formation of intra- and extra-articular adhesions, destruction of the cartilage becomes complete, and in the more progressive cases bony ankylosis ensues.

A brief description of some of the methods used for the correction of the more common deformities will be given, but for full information on this subject the reader is referred to the works of those orthopædic surgeons who have made a special study of the chronic rheumatic diseases (R. B. Osgood, A. G. Timbrell Fisher and H. Platt).

*Flexion of the Hips and Knees.*—There are several methods in use for the correction of this deformity. Except in very severe cases the hip joints are rarely seriously involved in rheumatoid arthritis, but they are maintained in flexion by the deformity of the knees. In cases of long duration, shortening and fibrosis of the quadriceps and other muscles may occur and give rise to a secondary flexion deformity of the hips.

*Weight Extension.*—The limb is placed in a modified Thomas' splint and about 10 to 15 lb. extension applied in the usual way. If a Balkan beam is available the limb in the splint is slung from this. This method does nothing to allay muscular spasm and the patient may experience considerable pain. The weight is removed once daily for movements of the joint and the application of massage and Faradism to the muscles.

*Serial Plasters.*—One of the most important advances in the technique of correction of deformities is the use of serial plasters (see Appendix). It is of particular value for the correction of flexion deformities of the knees, but can be used in any joint which is accessible to the application of plaster. In the case of the knees, a complete plaster is applied to the limb and bivalved when dry to allow of movement of the joint and massage to the muscles. After three to six days' complete rest in the plaster, it is found that the knee is now capable of an extra few degrees of extension. This gain is consolidated by the application of a new plaster. After four to six plasters have been applied, complete extension will frequently have been attained. In more resistant cases manipulation under a general anæsthetic may be required before a full range of movement can be restored to the joint. The advantages of serial plasters are that no strain is thrown on the articular structures, the muscles are put at rest, spasm is overcome and pain is relieved.

*Wedge Plasters.*—This is a modification of the serial plaster method. A rather heavier plaster is applied with an anterior slab over the knee to act as a hinge. Twenty-four hours after application the plaster is sawn through three-quarters way round at the knee, leaving the anterior slab intact. Every two or three days wedges are inserted behind the knee. Great care must be taken not to put too great a strain on the joint by forcing in too large wedges. The wedges merely "take up the slack," i.e., maintain the extension gained by passive relaxation of spasm and stretching of adhesions. The wedge plaster, therefore, simply takes the place of a number of serial plasters, the advantage being that only one or two plasters are required. Some obstinate cases which do not respond to serial plasters do well with this method. The great disadvantage is that the treatment of the muscles is impossible while the plaster is in position. In any type of plaster immobilization, exercises in the form of static contraction of the quadriceps muscles and active movement of the toes should be carried out for short periods at regular intervals throughout the day.

*Manipulation.*—Manipulation under a general anæsthetic is of value in properly selected cases of rheumatoid arthritis. Certain criteria must be observed. The first and most important is that the active phase of the



disease must be past. X-ray films of the joints must be studied carefully and bony ankylosis excluded. Subluxation is also a contraindication in most cases. Although a joint cavity may still be present in the knee, the patella may be firmly ankylosed to the lower end of the femur, and unless this can be mobilized little functional gain will be obtained from manipulation of the joint. Great care must be exercised if the bones are markedly decalcified, otherwise a fracture may result. Certain joints react well to manipulation—knees, hips and shoulders. Results are less certain in the wrists and ankles and good seldom comes of manipulation of the elbows. The presence of severe cartilaginous damage may not preclude some return of movement, but the after-treatment must be prolonged and weight-bearing avoided for some weeks.

When minor degrees of pain and disability are present, local infiltration of the peri-articular structures, on one or more occasions, with  $\frac{1}{2}$  per cent. solution of procaine according to the technique described for the treatment of fibrositis (see p. 833), followed by heat and movements, may be sufficient to banish pain and restore full function.

The intra-articular injection of a variety of substances has been recommended, but the results in rheumatoid arthritis have not been striking. Strict asepsis must be observed, and this method should only be used in hospital. More promising results have been obtained in osteo-arthritis (see p. 826).

In cases where abduction has become limited in the shoulder but where the degree of activity precludes manipulation under an anæsthetic, full movement may be restored by the use of an aeroplane splint. When first applied it is adjusted so as to hold the arm in the position of maximum abduction compatible with comfort. The arm is bandaged firmly to the splint, which must be well padded. The rest obtained will relax spasm and in a few days more abduction becomes possible. The splint is now adjusted to hold the arm in the new position. This process is continued until full abduction has been restored. The underlying principle is exactly similar to that of the serial plaster method. Heat and movement to the joint and massage and exercise for the muscles are employed daily.

In more severe cases the damage to certain joints may be of such a degree that appliances are necessary to supplement the impaired function before the patient can regain the power to walk. The simplest of these is crutches, which serve a useful purpose in the transitional stage between recumbency and unaided weight-bearing. It is important that they should be of the correct length for the individual patient, otherwise they may be the cause of further deformity, especially of the spine and hips. Another simple method of supporting an unstable joint is the application of a firm bandage, preferably crêpe. This will serve the double purpose of lending support and preventing over-movement, especially in the knees and ankles. When the knees are incapable of supporting the patient's weight it becomes necessary to fit a walking calliper splint. This should be furnished with a locking device at the knee which permits flexion when the patient wishes to sit down. Similar splints are used for taking the weight off a damaged hip, but they must be fitted with great care by a skilled technician, otherwise they will prove more of an encumbrance than a help. For less severe degrees of disability in the knee laced elastic kneecaps are useful when the objects are to provide light support and to prevent over-movement. These should



be provided with jointed metal side-pieces if additional stability is necessary. Anklets of a similar type are available.

When a marked degree of flat foot is present special shoes are necessary. They should not cause constriction and the heels should be carried forward  $\frac{1}{2}$  in. further on the inner side than on the outer, and also be raised on the inner side of the sole ("crooked" shoe). When collapse of the transverse arches of the feet cause metatarsalgia, a metatarsal bar should be fitted in addition in order to relieve pressure on the heads of the metatarsal bones. Considerable relief from pain may also result from the use of small pads of chiropodist's felt over the metatarsal heads together with the application of adhesive plaster round the foot, immediately proximal to the heads of the metatarsals.

In the very rare cases of rheumatoid arthritis in which the spine becomes involved, or where the posture is very bad, it may be necessary to fit a spinal brace. Here, again, expert opinion is required regarding the particular type of brace suitable for each individual case.

In the chronic stage of rheumatoid arthritis it is of paramount importance to prescribe a carefully-thought-out scheme of exercises, both for the correction of faulty body mechanics and for the restoration of function after deformity has been corrected. Details of exercises of value for these purposes will be found in the Appendix.

From what has been said in this section it will be appreciated that the correction of faulty body mechanics, the restoration of muscular tone and movement and correction of deformity in various joints, constitute an essential part of the co-ordinated plan of treatment. The physician in charge of the case should enlist the help of the orthopædic surgeon, whose special training and experience in these fields will enable him to give invaluable help to the patient.

## OSTEO-ARTHRITIS

For the definition and prophylaxis of osteo-arthritis see pp. 802, 805.

Treatment of the established disease is in the main palliative, since it would be unreasonable to expect that degenerated cartilage or bony out-growths can be repaired or removed by drugs, vaccines or physiotherapy. Treatment may be divided into (1) general, which includes the removal or correction of ætiological factors; and (2) local.

**General Treatment.**—If the patient is suffering severe pain in a weight-bearing joint such as the hip or the knee, the best method of taking the strain off the joint and relieving the pain is to confine the patient to bed for a week or two. During this period active non-weight-bearing exercises should be prescribed. Patients with severe pain have frequently reached this state by accepting the advice of their friends or medical attendant, that the best treatment is to "walk it off" otherwise the joint will become stiff. Not only is this advice unwise, but it is also inaccurate, since ankylosis does not occur in osteo-arthritis. For patients with less severe pain, modified rest should be ordered to meet the individual requirements of the case. Short walks on level turf may be allowed with benefit, but walking on hard or uneven surfaces for any distance must be discouraged. If exercise leads to an increase in pain or stiffness, too much has been done and the distance allowed must be reduced. If the patient is unable to accept this advice because of

his occupation, the mechanical devices discussed below may be of value in relieving the strain of weight-bearing in an individual joint. The occupational factor, as has already been mentioned, is of great ætiological importance in all chronic rheumatic diseases including osteo-arthritis, and the doctor must discuss with his patient the question of whether it is possible to change or modify his occupation should it be unsuitable. Similar advice may have to be given regarding hobbies or pastimes, such as golf, fishing and shooting, which may throw an undue strain on the affected joints.

Obesity is commonly present in individuals with osteo-arthritis, and reduction of weight by suitable dietotherapy is of great importance (see p. 383). If the obesity affects the abdomen particularly, the patient tends to assume a posture which throws still greater strain on the weight-bearing joints, and exercises for the correction of bad posture (see Appendix) should be carried out regularly.

If clinical evidence of thyroid deficiency is also present, as is not infrequently the case in women at the menopause, thyroid extract should be prescribed in suitable doses.

A regular motion of the bowels should be ensured by an adequate fluid intake and the use of ample fresh fruit and vegetables in the diet, assisted when necessary by a small dose of salts in the morning.

A conservative attitude should be adopted towards septic foci and their eradication, as osteo-arthritis is not believed to be the result of infection. Nevertheless, obvious septic foci should be removed, both on the grounds of general health and because of the possibility of their accelerating the degenerative processes in the joints.

**Drugs** play only a small part in the treatment of osteo-arthritis. Analgesics (see p. 810) are prescribed when necessary for the relief of pain. Potassium iodide, arsenic, guaiacum and sulphur (p. 811) have been recommended as of some value in a proportion of cases. Their mode of action is not any clearer in osteo-arthritis than in the other chronic rheumatic diseases and there appears to be no sound reason for their employment. For a critical evaluation of drugs used empirically see p. 811. Gold salts which are of use in rheumatoid arthritis are valueless in osteo-arthritis and fibrositis. Similarly vaccines and non-specific protein shock therapy play no part in its treatment.

**Local Treatment.**—Physiotherapy and not drug therapy is the essential feature of the treatment of osteo-arthritis. By this means, muscular spasm can best be relaxed, pain relieved and the circulation of blood and lymph in the neighbourhood of affected joints improved, with the hope that the degenerative processes may be retarded. Physiotherapy enables movements of the joints to be undertaken more freely with concomitant improvement of function. If a single joint is affected, such as the knee, considerable relief may be obtained from the local application of heat. Any of the methods described on p. 839 may be used, but mud packs are of particular value. In deep-seated joints such as the hips or spine the analgesic effects of heat may be best attained by means of diathermy or short-wave therapy. It has been claimed recently that beneficial results can be obtained in a high proportion of cases by deep X-ray therapy. In our experience definite symptomatic improvement resulted in about 50 to 60 per cent. of cases in a carefully controlled series. Accordingly, we believe that deep X-ray therapy is worthy of a trial in cases which have resisted the simpler and less expensive methods.

Massage should be given to the muscles surrounding the joint with a view to improving the local circulation and dispersing fibrositic lesions which are frequently present. Massage should not be applied to the joints themselves as it has no beneficial effect and may even prove harmful. Where wasting of muscle is present active exercises of the non-weight-bearing type should be prescribed.

Hydrotherapy (see p. 819) is of the greatest value in osteo-arthritis, particularly the deep-pool bath in which the patient can move his limbs under warm water, which relaxes spasm and eliminates the effect of gravity, thus enabling movements to be carried out with the minimum of pain. The undercurrent douche should be applied at the same time.

For those unable to visit a spa, a hot bath at home, medicated or otherwise (see p. 821), is a useful substitute in enabling the patient to obtain the benefits of heat and movement.

The injection of various substances into the joint cavities in osteo-arthritis has been practised for many years. Good results have been claimed following the use of lipiodol, gomenol, and novocaine. More recently, Waugh has recommended the use of a solution containing lactic acid and procaine (lactic acid 0.2 per cent. in 2 per cent. procaine). He bases this treatment on his observations on the *pH* of the synovial fluid. In normal fluid the *pH* is said to be 7.4 to 7.6. In osteo-arthritis it tends to become alkaline. Acidification of the fluid is claimed to favour the regeneration of cartilage. Injections are given at weekly intervals. The quantities advised are 15 to 20 c.c. for the hip joint and 10 c.c. for the knee. Smaller amounts are injected into other joints. The joint is gently manipulated after each injection. The patients are instructed to perform simple non-weight-bearing exercises daily. It is claimed that marked relief of symptoms is obtained in 50 to 60 per cent. of cases. How much of the benefits produced are due to the change in *pH* of the synovial fluid and how much to the effects of the local anæsthetic followed by manipulations is at present uncertain. Recent work suggests that equally good results may follow the use of procaine or normal saline. Other observers state that results are more lasting when lactic acid is used. Intra-articular injections of procaine solution with or without lactic acid can be given to out-patients. The procedure is simple, and the patient can usually continue at work. There is no certain way of deciding which patients will receive benefit. Treatment should be continued as long as improvement is being obtained. Methods of puncturing the cavities of joints are described on p. 953.

**Orthopædic Procedures.**—Manipulation under a general anæsthetic may be a valuable procedure, but it must be employed with great caution and only in selected cases where there is considerable pain and limitation of movement with only moderate bony changes. In such a case, peri-articular adhesions and capsular thickening are believed to be largely responsible for the disability which is present and much benefit may be obtained from manipulating the joint in a gentle manner under full surgical anæsthesia. This must be followed by daily movement of the joint preceded by heat.

Mechanical appliances for the relief of weight-bearing joints may be necessary if the measures already outlined fail to give relief. The types most frequently used are caliper splints constructed to take the weight off the knee or hip or a steel brace to support the spine. These appliances are expensive and should only be ordered on the advice of a competent ortho-

pædic specialist and should be fitted by a trained technician. The indications for surgical treatment are discussed on p. 837.

## CHRONIC MENOPAUSAL ARTERITIS

*(Chronic Villous Arthritis, Climacteric Arthritis)*

There is a form of arthritis which occurs commonly in women about the time of the menopause. Those affected have, as a rule, been considerably overweight for some years and show signs of the subthyroid state. The joints principally affected are the knees, but minor changes are usually present in the hands. In the early stages of the disease the affected joints are swollen and painful owing to thickening of the peri-articular structures, hypertrophy of the synovial membrane or less commonly to the presence of fluid in the joint cavity. The condition is a proliferative synovitis rather than an arthritis, since X-rays reveal little or no bony change. In untreated cases the disease slowly progresses until typical signs of osteo-arthritis occur.

Various factors appear to play a part in the ætiology of this disease, but the most important from the point of view of treatment is obesity. Menopausal endocrine deficiencies may influence the onset directly by giving rise to premature senility and the early appearance of degenerative changes in the joints, or indirectly by leading to obesity.

The condition is one which is peculiarly amenable to treatment in the early stages. The first step must be to reduce the strain thrown upon the knees by excessive weight. If this object is attained by careful regulation of the diet, and, where necessary, by the administration of thyroid, combined with suitable general and local treatment, the appearance of the cartilaginous and bony changes of osteo-arthritis may be indefinitely delayed. A suitable diet of low calorific value is prescribed, and the patient must be impressed with the importance of adhering to it strictly. For details of a suitable diet see p. 387. A small dose of thyroid, such as  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) twice a day, should be administered with the object of correcting any endocrine deficiency and to augment the effect of the reducing diet. The dose must be adjusted to suit the requirements of each individual case. Drugs have little beneficial effect in chronic menopausal arthritis with the exception of the analgesics. The peripheral circulation is often sluggish and the skin is tacked down to the subcutaneous tissues. Tender fibrositic areas are commonly present around the joints and in the scapular region. Hydrotherapy and the other methods of applying heat followed by massage, as already described on p. 819, do much to improve the circulation, disperse the fibrositic thickenings and restore the function of the joints. Adequate rest to the joints themselves must be insisted on, walking being reduced to a minimum for some weeks, until the swelling and pain have greatly subsided and a substantial reduction in weight has been secured. Crêpe bandages or elastoplast should be applied to the knee in order to maintain an even pressure, which will aid the reabsorption of effusion and provide support during weight-bearing. These should be retained when the patient returns to active life and until the quadriceps muscles have regained their normal tone. Static muscular contractions should be practised during the time when the patient's activities are restricted. Spa treatment is particularly suitable for patients with menopausal arthritis as the physiotherapeutic

and hydrological facilities available are of the utmost value. When very marked synovial proliferation is present, resulting in nipping of fringes between the articular surfaces, surgical intervention may become necessary (see p. 837).

Excellent results are to be expected from the use of deep X-ray therapy in this disease. If the treatment is employed in the early stage, before radiological evidence of osteo-arthritis has appeared, complete cure follows in a proportion of cases. In more advanced cases the progress of the disease may be arrested and relief of symptoms may result. As a rule more than one course of treatment is required. The prescription of dosage and the length of the course should be in the hands of a radiologist skilled in the use of deep X-ray therapy and familiar with its application to diseases of the joints.

When the disease is treated early the prognosis is good. If osteo-arthritic changes are established when the patient is first seen, the treatment is the same as already described for that disease on p. 824.

### SPONDYLITIS

Arthritis affecting the spine occurs in two main forms—spondylitis osteo-arthritica (spondylosis deformans) and ankylosing spondylitis (spondylose rhizomélque, spondylitis ankylopoietica).

**Spondylitis Osteo-arthritica.**—The ætiology and pathology of osteo-arthritis affecting the spinal articulations are identical with those of osteo-arthritis arising in any other joint. It occurs in those whose occupation has thrown a strain on the back over a period of years. It is a slowly progressive condition and marked degenerative changes may be present before symptoms appear. It is often discovered in people past middle life during the course of a routine examination. Trauma, obesity, occupation and postural defects may all play a part in conditioning the onset of symptoms, and these factors should receive attention in the early stages of the disease.

When symptoms arise they are due to pressure of osteophytes on nerve roots or to reactionary fibrositis in the surrounding muscles and ligaments. Pain may be severe but is often absent, and in more advanced cases muscular wasting and disturbances of sensation may manifest themselves owing to pressure on nerve roots.

In milder cases, where pain is mainly due to fibrositis of the spinal muscles, the application of hot packs over the affected area will give relief. Massage should not be prescribed until the more acute symptoms have subsided, when it may be used with benefit. At this stage the various forms of baths already described are valuable. In more severe cases, where pressure on the nerve roots is causing neuritis, the patient should be put to bed and the spine kept flat by the insertion of fracture boards under the mattress. Where arthritis of the cervical spine is giving rise to brachial neuritis, relief may be obtained by applying weight extension. The weights are attached to a cord running from a head sling through a pulley at the top of the bed. Ten to fifteen pounds are usually sufficient. In less severe cases adjustment of the number of pillows used by the patient may be of value. Local heat should be used in one or other of the forms already described.

In cases of osteo-arthritis of the spine which fail to respond to these simple measures, repeated courses of deep X-ray therapy are beneficial in a proportion of cases.

**Ankylosing Spondylitis.**—This is a disease mainly of early adult life and is much more common in males. Its incidence is relatively small, but when it arises it is an extremely serious condition which may completely incapacitate the sufferer and even endanger life. The pathology is that of infective or atrophic arthritis, and it has been called rheumatoid arthritis of the spine, although in the opinion of a number of observers it is an entirely different disease. The onset of symptoms referable to the spine is preceded by a period during which the patient complains of vague pain in his muscles and joints. The estimation of the sedimentation rate at this time may suggest the presence of some infective process, and X-rays of the spine and pelvis may show the early changes of ankylosing spondylitis. The disease affects particularly males in the early twenties, well developed and of an active mode of life. In the majority of cases the first joints to show radiological changes are the sacro-iliacs, which become ankylosed very early in the course of the disease. As the disease progresses the intervertebral and costovertebral joints are involved, the spine becomes rigid and the thoracic cage immobile. In a few severe cases the disease may spread to involve the hips and shoulders, more rarely the elbows, hands, knees and feet. The joint changes are accompanied by generalized muscular wasting. In the early stages patients are usually ambulatory, with the result that, owing to decalcification and softening of the vertebral bodies, the spine assumes a kyphotic position, and unless treatment is instituted early this deformity will become permanent owing to the deposition of calcium in the ligaments and capsules of the joints. The calcification and later ossification of the joint capsules is a characteristic feature.

*General Treatment.*—The disease is believed to be infective in origin, and a scheme of treatment exactly similar to that described in the section on rheumatoid arthritis must be adopted (see p. 806), including rest in bed in the active stage to overcome fatigue and prevent deformities, and the application of all the measures already detailed to raise the general resistance and improve the health of the patient. A careful search should be made for septic foci in the teeth, tonsils, etc. At one time the view was widely held, especially in France, that the gonococcus was the causative organism in ankylosing spondylitis, but the negative history and the absence of bacteriological evidence in many cases do not uphold this view.

The value of vaccines, gold and protein shock therapy is as much a controversial subject in ankylosing spondylitis as it is in rheumatoid arthritis. Clinical experience suggests that gold is not so effective in ankylosing spondylitis as in rheumatoid arthritis. If used at all it must be given with great care.

Drugs should be used with discretion as in rheumatoid arthritis, analgesics again being the most valuable.

*Local Treatment.*—The results of X-ray therapy in this disease are very satisfactory. Its value is so great that it should be used in every case, whatever the stage of the disease. Even in advanced cases with established deformity, pain may be markedly relieved. The best results follow a course of daily treatment lasting two weeks. Treatment is applied to the whole spine and sacro-iliac joints. Even in very early cases it should never be confined to the lumbar spine and sacro-iliac regions. The skin dose on all fields is 2,500 r. The course should not be repeated except in special circumstances, but should the hips or shoulders become painful at a later date,

further radiation may be applied to these joints. In young women, the sacro-iliac regions should be avoided in view of the danger of causing sterility.

In early cases with no deformity the disease process may be completely arrested and full movement may be regained. The maintenance of good posture must be assured. When radiological changes are confined to the sacro-iliac joints no period of rest in bed may be necessary, but postural and breathing exercises must be performed daily. If, at the end of one year, there has been no recurrence of symptoms, routine exercises may be discontinued. In more advanced cases, where X-rays show no ossification of the spinal ligaments, but where posture is already poor, a period of two to three weeks' rest in bed combined with postural exercises is necessary. Fracture boards should be placed under the mattress. On getting up, these patients should be fitted with a spinal brace, which should be worn until muscular power has been completely restored. The brace is removed several times daily and active exercises performed. In advanced cases with established deformity, the relief of pain and stiffness following X-ray therapy greatly facilitates the restoration of good alignment by the use of serial plaster shells. These patients may have to wear some form of orthopædic support permanently. Recognition of the disease at an early stage, followed by adequate treatment, will effectively prevent the occurrence of such late manifestations.

Even in cases in which the disease appears to be completely arrested, medical supervision should be continued to ensure the maintenance of good posture.

### STILL'S DISEASE

A rheumatoid type of arthritis occurs occasionally in children between the ages of three and ten. It is accompanied by fever, glandular enlargement and splenomegaly. There is a tendency for the infantile proportions of the limbs to persist, probably due to interference with normal growth by the disease processes. The findings in the joints do not appear to be specific for the disease but common to all types of chronic infective arthritis. The disease tends to run a prolonged course. Although dramatic remissions have been recorded occasionally following the eradication of a septic focus or the use of gold therapy, the results of treatment are generally held to be less satisfactory than those obtained in ordinary rheumatoid arthritis.

### NON-ARTICULAR RHEUMATISM

#### *(Fibrositis—Muscular Rheumatism)*

**Definition.**—Fibrositis may be defined on clinical grounds as a syndrome characterized by pain, aching and stiffness, affecting essentially the structures related to the locomotor system. Pain and stiffness are usually worst after a period of rest, and although movement initially increases pain, a period of mild exercise frequently gives relief. Tenderness may be diffuse, but careful search will often reveal the presence of well-localized painful areas, the so-called myalgic spots. In a proportion of cases nodules are palpable, some of which are acutely tender on pressure. There is rarely any systemic upset, and radiological examination is negative. Until recent years it was believed that the underlying pathology of the syndrome was an inflammation of the white fibrous tissue, but considerable doubt has been cast on this

hypothesis. In chronic cases, however, changes in fibrous tissues of a non-specific type, resulting from the action over a period of time of various ætiological agents discussed below, may explain the persistence of residual symptoms. Hyperplasia of fibrous tissue seems to be the most likely cause of the persistent limitation of movement seen in old-standing cases. In acute cases the demonstration of well-localized tender spots suggests that these may be the primary lesions and that diffuse aching and stiffness are reflex in origin. The fact that the injection of a local anæsthetic into these so-called myalgic lesions frequently leads to dramatic relief of symptoms would appear to lend colour to this view. The origin and pathology of these lesions have not been fully elucidated. Copeman and Ackerman have shown that at least some of these lesions consist of lobules of fat which have herniated through fascial planes and give rise to pain consequent on strangulation and œdema.

Since measures for the prevention and treatment of fibrositis are based essentially on a knowledge of the ætiological factors involved, it is considered appropriate to discuss briefly those believed to be of primary importance.

**Ætiology.**—Although the ætiology of fibrositis is still unsettled, common experience has shown that certain factors are of particular significance. More than one may be concerned in the individual case, and until all are adequately dealt with treatment may produce only temporary alleviation of symptoms, to be followed by relapse on resumption of an unsuitable occupation or return to an uncongenial environment.

**Cold.**—Exposure to cold and damp are universally recognized as factors which commonly precipitate an acute attack of fibrositis, especially in those people with a predisposition to the disease. This is particularly the case if the patient becomes chilled after physical effort or is exposed to a draught which causes a sudden drop in the local skin temperature.

**Physical Fatigue.**—Fatigued muscles are peculiarly prone to become the seat of an attack of fibrositis. Chronic fatigue brought on by continued over-use of specific muscle groups is more important in this respect than general fatigue following excessive physical exertion. This probably explains the high incidence of fibrositis in certain occupations where long-continued repetition of certain movements is common.

**Trauma.**—The effects of trauma and fatigue cannot be clearly separated. Fatigued muscles are prone to injury, and the effect of continued use of exhausted muscles may result in rupture of individual fibres. Fibrositis is certainly a common cause of disability in heavy industry.

**Posture.**—Poor posture is associated with muscular imbalance, which results in chronic local fatigue of certain muscle groups. Such local fatigue is accompanied by dull aching pain, often diagnosed as fibrositis. Local treatment in such cases is of value only if accompanied by correction of faulty posture. Poor posture, however, undoubtedly predisposes the patient to acute attacks of fibrositis in chronically fatigued muscles. It should be remembered that postural strains occur both in obese and slender subjects.

**Infection.**—Muscular pain and tenderness are prominent features in the acute phase of many general infections. It is less commonly recognized that tender areas in the muscles may persist after such infections and form a basis for future attacks of fibrositis. Epidemics of "stiff neck" have been reported recently in this country among industrial workers. This form of epidemic myalgia is believed to be due to a virus infection.



The fashion of incriminating a focus of infection in fibrositis is now less popular, but in a proportion of cases symptoms have only cleared up following the removal of infected tonsils, teeth, etc. This possibility must be borne in mind in cases which fail to respond to adequate treatment or where attacks have been repeatedly associated with acute infections.

*Metabolic Disorders.*—In a few cases of fibrositis unassociated with articular symptoms, there appears to be a gouty basis for the condition, and estimations of the blood uric acid reveals figures persistently above normal. These cases are usually of a chronic nature. A definite association between attacks and the indulgence in certain types of food or drink may give a clue to the diagnosis. Attention to diet and the administration of the drugs used in gout (see p. 851) will be an important feature in their treatment.

In the majority of cases of fibrositis there is no satisfactory evidence of disordered functions of the endocrine glands. In some cases of hypopituitarism and hypothyroidism painful areas in the subcutaneous tissues occur (panniculitis). The routine administration of endocrine preparations is to be deplored.

A few words must be said at this stage about certain conditions where a diagnosis of fibrositis is only too commonly made and where such a diagnosis may lead to marked prolongation of disability.

*Psychoneurosis.*—Many patients complaining of muscular pain and stiffness have no local organic basis for their symptoms, which are an expression of emotional tension or mental conflict. The use of physical methods of treatment in such cases is absolutely contraindicated since they perpetuate the belief in the patient's mind that physical causes are responsible for his symptoms, thus making cure by psychotherapy much more difficult to accomplish.

*Referred Pain.*—It has been clearly shown that lesions in deep structures can give rise to pain and spasm in anatomically related muscles and in muscles distant from the lesion but with a nerve supply from the same segment of the cord. These symptoms may mask the presence of the primary lesion and lead to an erroneous diagnosis of fibrositis. In these cases local treatment of the painful muscles may give sufficient relief to perpetuate the mistake.

**Summary.**—From what has been said above, the term "fibrositis" used in clinical medicine covers a variety of lesions of known and unknown ætiology which give rise to pain, stiffness, aching and limitation of movement.

The diversity of the causes of such symptoms emphasizes the need for a careful history and a complete physical examination in every case. The application of a rigid clinical discipline will reveal causes capable of correction in many cases. In addition it will eliminate cases of functional and reflex origin which would otherwise be labelled fibrositis and relegated to the physiotherapy department, a procedure harmful both to the patient and the physician in charge of the case.

## TREATMENT

**Acute Stage.**—In the absence of an accurate knowledge of the underlying pathology, treatment of the acute attack of fibrositis must still be based to some extent upon empirical methods. If pain and spasm can be relieved, active movements can be started earlier, and disability may be cut short. General and local measures should be combined to achieve this object.

Analgesics should be prescribed in full doses. Aspirin in doses of 15 gr. (0.9 gm.) combined with 5 gr. (0.3 gm.) of phenacetin and  $\frac{1}{4}$  gr. (15 mg.) of codein four-hourly will suffice in most cases, but in severe lumbago a single dose of morphia, gr.  $\frac{1}{4}$  (15 mg.), may be necessary to control the pain. Tension should be removed from the painful structures by arranging the patient in bed in the position of greatest comfort but which permits the application of local remedies. Heat should be applied locally by any of the methods described on p. 817 and in the Appendix (p. 839). The method of choice will be that which can be most conveniently applied to the affected part. There is much to be said for the use of simple methods available in any household (hot-water bottles, linseed or kaolin poultices, the use of a hot iron over a towel), as they can be applied with the minimum of delay. In many cases these measures will give marked relief within a few hours, and it will become possible to locate the acutely tender areas which are believed to be the trigger points or primary myalgic lesions. It must be borne in mind that these tender points may lie outside the area in which the patient feels his pain, but pressure on them will reproduce the symptoms of which he complains. These areas should be infiltrated with a few c.c. of  $\frac{1}{2}$  per cent. procaine in normal saline. Accurate location is essential and a final decision on the site of injections should only be made when typical pain is produced by the needle point. Gentle massage should be applied to the areas injected, followed by heat. As soon as the pain has been relieved and spasm relaxed, gentle active movements should be encouraged. Dramatic relief may follow this régime and the patient may be able to resume his ordinary activities almost at once. The treatment should be followed up by a course of heat, massage and exercises. If the best results are to be obtained, treatment should be administered daily for at least a week. A thorough inquiry into possible ætiological factors should be made and common-sense advice given as to how their effects can be mitigated. The avoidance of chilling is important in every case, and in patients subject to recurrent acute attacks and whose work involves exposure to cold and wet, especially if combined with general or local muscular fatigue, a change of occupation may be in the patient's best interests. A conservative attitude towards focal sepsis is wise. This question is discussed on p. 808. No particular dietetic régime need be advised except in cases when clear evidence of a gouty basis or an idiosyncrasy to a particular food is obtained, or when obesity is present. Advice on suitable clothing, exercise in the fresh air and regular baths should always be given (see p. 807).

**Subacute and Chronic Stage.**—A proportion of cases continue to complain of residual symptoms after the acute attack has subsided. Others never experience an acute attack but suffer from continuous or recurrent pain and stiffness of a less intense degree. Such people are usually sensitive to impending changes in the weather and suffer most during cold, wet spells. It is amongst this group that diagnosis is particularly difficult. Great care must be taken to differentiate between patients whose symptoms are functional in origin and those with a genuine organic basis for their disability. Disease of deep structures giving rise to referred pain and tenderness must be excluded by a complete physical examination supplemented by radiological or biochemical investigation when indicated. In chronic cases of fibrositis it is likely that some increase in fibrous tissue in and around muscles, tendons and joint capsules is responsible for the persistence

of pain and stiffness. Treatment of chronic fibrositis, to be effective, must be more vigorous and prolonged than in the acute case. Analgesics, heat, massage, local infiltration of painful nodules and exercise are the principal methods of treatment, but results are less dramatic. Accurate location and infiltration of tender areas is as valuable as in the acute phase, but injections may have to be repeated on several occasions and should be followed immediately by heat, vigorous deep massage and active exercises. Hydrotherapy is of real value in these cases since it combines heat, massage and active movement (see p. 819). The régime of a spa is particularly suitable for those patients who can afford it, but most of the benefits of spa treatment can be obtained at home by the intelligent application of the methods described and reorganization of the patient's way of life.

*Diet.*—There is no specific diet for chronic fibrositis. Obesity must be corrected. The following points should receive attention: (1) idiosyncrasy to any particular food or drink; (2) the presence of constipation; (3) clinical or chemical evidence favouring a gouty basis. In the exceptional case where there is evidence to support a dietetic or metabolic cause, a bland diet of a lacto-vegetarian type as used in gout (see p. 853) should be prescribed.

*Drugs.*—A large number of drugs have been recommended for chronic fibrositis, the most commonly employed being iodine, arsenic and sulphur. We believe that the beneficial effects claimed for the use of these drugs have been grossly exaggerated. Thyroid extract has a place in the treatment of the obese patient (see p. 391). Where a gouty basis exists, colchicine should be given a trial and the other measures put into effect as described on p. 851. Benefit has been claimed to result from protein shock therapy in resistant cases. For details of methods see p. 814.

*Convalescence.*—Rehabilitation following a severe attack of fibrositis should be thorough. A holiday at the seaside may suffice in milder cases, but thorough restoration of general fitness is required in those patients returning to heavy work. This may best be carried out in a residential or day-to-day rehabilitation centre where graduated physical training and games can be used to accomplish final hardening. Much subsequent invalidity and loss of working time may thus be avoided.

It is now proposed to discuss briefly the treatment of fibrositis in certain sites where diagnosis may be difficult or where special forms of treatment should be employed.

**Occipital Region.**—Fibrositis of the occipital aponeurosis may be a cause of troublesome headache. Examination will reveal the presence of tender points in the region of the occipital ridge. Pressure on these points causes pain, which radiates over the vault of the skull. Careful localization and infiltration of these trigger areas, followed by a short course of heat and massage, will usually give complete relief.

**Cervical Region.**—Fibrositis involving the cervical muscles is a frequent cause of painful stiff neck. Local chilling appears to be a peculiarly potent factor in precipitating the attack. The condition is commonly unilateral, causing wry neck, but both sides may be affected simultaneously. Movement is markedly restricted by pain and muscular spasm. Acutely tender areas are most frequent near the occipital attachment of the trapezius, the superior margin of this muscle midway between the acromion and the occiput, and in the clavicular portion of the sternomastoid. Infiltration of these points may give immediate relief. A careful examination of the ear,

nose, throat and teeth should be undertaken to detect focal sepsis. Should symptoms persist or attacks occur frequently, manipulation of the cervical spine may be successful, but possible reflex causes such as cervical arthritis, caries, or prolapsed intervertebral disc must be carefully excluded by clinical and radiological examination before this method is used. Heat, massage and active movement should be applied daily until full and painless movement has been restored.

**Shoulder.**—The potential causes of pain in the region of the shoulder are numerous and the differential diagnosis may be difficult. Root pain, radiating to the shoulder and down the arm, may arise from lesions within the spinal canal (tumours, brachial radiculitis, prolapsed disc) or disease of the cervical vertebrae causing pressure on the roots of the brachial plexus (caries, osteo-arthritis, spondylitis, osteomyelitis). Various conditions causing pressure on the cords of the brachial plexus must be distinguished (cervical rib or fibrous band, abnormal first rib, prominent anterior border of scalenus medius, contracted scalenus anticus, compression between the first rib and the clavicle when the shoulder is retracted and abducted). In all these conditions careful examination will reveal evidence of pressure on the roots or cords of the brachial plexus, and in the latter group compression of the brachial artery in certain positions of the arm. Movements in the shoulder joint will be unimpaired.

If acute traumatic conditions are excluded, the common causes of painful shoulder are

1. Supraspinatus tendinitis.
2. Subacromial bursitis.
3. Adhesive capsulitis.
4. Fibrositis of trapezius, supraspinatus, infraspinatus, deltoid or rhomboids.

*Supraspinatus tendinitis.*—The ætiology of this condition is unknown, but minor repeated trauma probably play an important part. In the early stage of the disease it is possible to move the shoulder passively through a full range of movement, but active abduction causes acute pain, which may disappear when the arm has been abducted beyond a right angle. Treatment consists of infiltration of the supraspinatus tendon near its insertion followed by heat and active exercises. In early cases this may lead to complete cure. In long-standing cases there is almost invariably an accompanying subacromial bursitis.

*Subacromial bursitis.*—Skiagrams may show deposits of calcium in the tendon and bursa. Abduction and rotation in the shoulder will be limited to a greater or lesser degree. Conservative measures should be given a trial. Infiltration of the bursa followed by heat and graduated exercises may lead to cure, but in many cases more radical measures are required. Deep X-ray therapy is said to give relief in some cases. Good results have been obtained by washing out the bursa with saline. In cases which fail to respond to these measures surgical removal of the calcareous deposits may be required. Whichever method proves necessary, function must be restored by graduated exercises.

*Adhesive capsulitis.*—Fibrositis involving the capsule of the shoulder joint is a common complication of the above conditions. It may arise independently following trauma. In the elderly it is a common complication of fractures of the arm, forearm or hand, when active movements of the

shoulder have been neglected during immobilization in plaster. Movement is best restored by a series of gentle manipulations under general anæsthesia. Between manipulations the arm is kept in an abduction splint and active movements encouraged. The condition can best be avoided by early and adequate treatment of painful lesions in and around the shoulder.

*Fibrositis of the muscles of the shoulder girdle* is treated by the methods already described—infiltration of myalgic spots followed by heat, massage and exercise.

**Thoracic Region.**—Fibrositis may involve the intercostal muscles, giving rise to severe pain. The absence of any systemic disturbance or friction rub on auscultation and the presence of localized superficial tenderness are helpful points in differentiating the condition from pleurisy or pain of cardiac origin. Treatment is along the usual lines, including local infiltration, but in severe cases it may be necessary to immobilize the affected side of the chest with strapping. It should be remembered, however, that the symptoms of herpes in the early stage may be indistinguishable from intercostal fibrositis.

**Lumbar Region.**—Pain and muscular spasm in the lumbar region may arise from many causes and may also present a difficult diagnostic problem. In the isolated incident, when acute pain follows unaccustomed exercise in cold, wet conditions, a diagnosis of fibrositis of the lumbar muscles or lumbago may be made with reasonable assurance. Treatment as described for acute fibrositis will lead to cure. In cases where acute attacks occur repeatedly, or where the patient complains of chronic backache, a careful search for the cause must be undertaken. X-ray examination of the lumbar spine and pelvis will exclude secondary carcinoma, congenital anomalies, caries, osteomyelitis, osteo-arthritis, spondylitis ankylopoietica, sacro-iliac arthritis, spondylolithesis, etc. Gynæcological conditions in women were held to be a frequent cause of backache in the past, but gynæcologists now state that gross abnormalities may be found in the absence of backache as a symptom. Referred pain from visceral organs is readily differentiated by the fact that there will be no restriction of movement in the spine—a constant finding in all the other conditions mentioned. The remaining and most important cause of chronic backache is now believed to be a lesion of an intervertebral disc. In the early stages of this condition the protrusion is small and does not give rise to pressure on a root. There is, therefore, no pain in the distribution of the sciatic nerve. Many of these cases are said to develop sciatica later on. Nearly all such cases in the past have been treated as chronic fibrositis of the lumbar muscles. A history of recurrent acute attacks precipitated by sudden movement, heavy lifts or twisting strains should suggest the presence of a prolapsed disc. Rest, including immobilization in plaster when necessary, should form the basis of treatment in these cases in the first instance. Surgery should be reserved for those in which conservative measures have failed (see p. 837).

In cases believed to be fibrositic in origin, infiltration of tender areas, heat, massage and exercises will lead to improvement. In chronic backache every effort should be made to correct bad posture, as this factor alone will tend to perpetuate symptoms. (For suitable exercises see Appendix.)

#### SCIATICA

Pain in the distribution of the sciatic nerve may arise from causes too numerous to mention, but for simplicity it can be divided into two types:

(1) pain caused by pressure on the roots of the lumbar plexus; (2) referred pain from lesions in the distribution of sensory nerves arising from the same segments of the cord as the sciatic nerve. In root sciatica the commonest cause is now generally believed to be protrusion of the intervertebral discs between L4 and L5 or L5 and S1, but other causes such as intra- and extra-medullary tumours, tumours of the cauda equina, inflammatory or neoplastic disease of the vertebral bodies, osteo-arthritis of the spine, ankylosing spondylitis and pelvic tumours must be given consideration in the individual case. In sciatica of this type examination will usually reveal flattening or reversal of the lumbar curve, scoliosis, and some limitation of flexion. Neurological signs determined by the level of the protrusion of the disc are present in the majority of cases.

Sciatica of fibrositic origin is always of the referred type. Flexion of the lumbar spine may be limited, but reversal of the lumbar curve and scoliosis are rarely found. Sensory and motor signs are absent. The primary lesion may be fibrositis involving the lumbo-sacral or sacro-iliac ligaments, the gluteal or lumbar muscles or the hamstrings. Once the diagnosis of sciatica of the referred type has been made, treatment should proceed along the lines already indicated for fibrositis. Rest in bed is usually necessary. Pain should be relieved by full doses of analgesics and local heat. Local areas of tenderness should be infiltrated with procaine. When the more acute phase has passed, massage and exercises are prescribed. In severe cases, where the presence of a prolapsed disc can be excluded with confidence, epidural injection combined with manipulation of the spine under a general anæsthetic should be advised. This procedure has been used with considerable success by the authors but should only be carried out when conservative measures have failed. Special attention should be paid to the correction of poor posture in patients recovering from sciatica, as postural strains are believed to play an important part in the ætiology of the primary lesions. This view is confirmed by the observation that in young patients intractable sciatica may be caused by congenital shortness of one leg. The symptoms rapidly disappear when the boot on the affected side is raised.

## THE RÔLE OF SURGERY IN THE CHRONIC RHEUMATIC DISEASES

Before discussing the part played by surgery in the chronic rheumatic diseases, it must again be emphasized that early and adequate treatment will, in the vast majority of cases, obviate the necessity for surgical procedures. Surgery has no place in the treatment of the acute or subacute stages of rheumatoid arthritis, but offers to an arthritic derelict who has failed to respond to physiotherapeutic measures the only hope of regaining some degree of useful function.

Before surgical measures are considered in the treatment of rheumatoid arthritis certain criteria must be observed. These have been clearly defined by Pemberton and Osgood as follows :—

1. Arrest or quiescence of the disease.
2. Preliminary treatment to improve the patient's general condition as much as possible.

3. Correct appraisal of the patient as an operative risk.
4. A knowledge of the patient's psychology and a belief in his ability to maintain morale.
5. An accurate estimate of the number and nature of the operations which will be required to attain the functional objective.
6. Provision for carrying through the entire operative campaign. This includes (a) special hospital facilities and optimistic, experienced nursing; (b) consideration of the patient's financial resources in relation to after-treatment, especially physical therapy and prolonged "follow-up."
7. Thorough training in joint surgery, good judgment and meticulous technique on the part of the surgeon.

In rheumatoid arthritis deformities requiring surgical correction may be present both in arms and legs. When this is the case the arms, as a rule, should be dealt with first, as the psychological effect on the patient of being able to feed herself and attend to her toilet is valuable in fortifying her for the more serious and time-consuming procedures required for the restoration of the ability to walk.

It is not proposed to give details of the various operations, but merely to mention the object of each and the type of case on which they can most profitably be performed.

**Synovectomy.**—This type of operation is indicated in cases of rheumatoid arthritis and occasionally in cases of menopausal arthritis, where other forms of treatment have failed to reduce swelling and disability, and recurrent effusion and pain result from the nipping of tags of proliferated synovial membrane between the articular surfaces. The operation consists in the removal of as much as possible of the hypertrophied synovial membrane in the affected joint.

**Capsulotomy.**—This operation consists of the division of contracted ligaments and joint capsules which are causing flexion deformities but where a free range of movement exists up to the position of deformity. It is particularly applicable to the knee-joints, but may be used in other joints.

**Arthrotomy.**—In rheumatoid arthritis an isolated mass of proliferated synovial membrane may give rise to disability as a result of being pinched between the articular surfaces during movement of the joint. In osteo-arthritis individual chondro-osseous spurs may limit motion, or loose bodies may be present in the joint cavity. In these conditions arthrotomy may be required for their removal. The existence of extensive articular damage is not necessarily a contraindication to the operation, because relief of acute symptoms may be obtained.

**Osteotomy.**—Osteotomy is employed for restoration of the normal alignment of joint surfaces when a useful range of movement is still present in the joint, or for the correction of mal-alignment in a joint which has already become ankylosed. For example, osteotomy may serve a useful purpose in correcting the flexion and adduction deformities which are common in more advanced cases of osteo-arthritis of the hip joint.

**Drilling of the Head of the Femur (Forage).**—This procedure is no longer employed.

**Acetabuloplasty.**—In this operation the upper and anterior parts of the acetabular margin are removed on the basis that pain may occur in osteo-arthritis due to the contact between the neck of the femur and the hyper-

trophied rim of the acetabulum on abduction. The operation is of real value in selected cases.

**Arthrodesing Operations.**—When a joint has become unstable and useless from a functional point of view, considerable benefit may be derived from a procedure which deprives it of all motion but renders it stable. A joint may still be capable of a limited range of movement, but be so painful that from the patient's point of view the movement can be put to no useful purpose. Here, again, artificially produced ankylosis may banish pain and enable the patient to use the limb. This type of operation is of value in selected cases of both rheumatoid and osteo-arthritis.

**Arthroplasty.**—In this operation the joint is completely exposed, the bone-ends remodelled and a piece of fascia interposed to prevent ankylosis and allow free smooth motion. A thin vitallium cup is sometimes used instead of fascia and the results are encouraging. In osteo-arthritis the operation is mainly applied to the hips. Arthroplasty of the hip is a serious operation from the standpoint of shock and many surgeons prefer a McMurray sliding osteotomy. In carefully selected patients with rheumatoid arthritis whose general condition is good, and who will co-operate willingly in the long post-operative period required to secure a functionally good result, arthroplasty is believed to have a wider application than was hitherto thought. A high degree of surgical skill is essential and infinite patience on the part of both the surgeon and the patient is required. Weight-bearing must be delayed for at least two months, and for several weeks longer it must be aided by crutches and a stabilizing apparatus applied to the joint. The best results are obtained in the elbow, knee and hip.

**Sympathectomy.**—In certain cases of rheumatoid arthritis the limbs are cold and clammy. A cervical sympathectomy in the case of the hands and a lumbar sympathectomy in the case of the feet will have the effect of rendering them warm and dry. In early cases some relief of pain and improvement in function may result, but the operations on the sympathetic system have a very limited application in rheumatoid arthritis.

This brief survey of the rôle of surgery in chronic arthritis may help to indicate that the outlook, even in the arthritic derelict, may not be so hopeless as has been previously thought. Success depends upon the close co-operation of physicians and surgeons who have made a special study of the problems presented by the chronic rheumatic diseases.

## APPENDIX

### METHODS OF APPLYING LOCAL HEAT

**Dry Heat.**—Salt or sand retains heat for a considerable period and may be used when other methods of applying dry heat are not available. The amount required varies with the part to be treated. Enough must be used to cover completely or enclose the group of muscles or joint affected by the disease. The substance is heated in a metal container over a fire or in an oven, and is applied directly to the part or filled into sand-bags which are then packed around it. Hot-water bottles of the rubber-bag variety can be applied to a painful area or moulded to a joint and are available in the majority of homes. They should be held firmly in place by a bandage or a flannel binder. Electrically heated pads which can be plugged into any electric-light socket can be purchased cheaply and are very handy. The



pad is applied over the part to be treated and the controlling switch turned to full. When the temperature begins to cause discomfort the current is reduced. These pads can be kept in position for two to three hours. The old-fashioned method of applying local heat by means of a hot iron over a towel or brown paper may afford relief in cases of fibrositis of the spinal and gluteal muscles. Radiant heat and infra-red lamps form clean and efficient sources of heat. An electric radiator or gas fire can be used if the patient cannot afford a portable lamp, and are satisfactory but not so handy. Exposure to radiant heat or infra-red rays should not exceed fifteen to twenty minutes at a distance of 2 ft. The time of exposure will vary in each individual case, depending on personal sensitivity, and care should be taken particularly with the first two or three exposures to avoid over-exposure, which may cause burns.

**Moist Heat.**—A simple method of applying moist heat is by means of a mud pack. Spa mud can be bought in the form of dried cubes or in a compress ready for use. Boiling water is added to the dried mud and the temperature adjusted to 110° to 115° F. The mud is then applied directly to the painful muscles or joints and covered with a waterproof sheet and a blanket. The pack remains in position for one to two hours. In the case of the mud compress it is dipped into hot water (temperature 120° F.), shaken and applied in the same way as the dried mud. Packs made from powdered Fuller's earth form a cheap and effective substitute for spa mud. The earth can be purchased in bulk for a few pence a pound. It is mixed with hot water, spread on calico or linen and applied as described above. Peat is also employed for this purpose and can be bought in convenient packages for home use. Another convenient method of applying local moist heat is the use of a kaolin poultice. The material is packed in tins and is heated by placing the tin and contents in a pan of boiling water. When thoroughly hot the contents are spread on calico or linen and applied as already described to the affected joint or muscle. It should be left in position for two to three hours.

**Paraffin-wax Baths.**—One of the best methods of applying local heat is by means of paraffin-wax baths. The wax can be obtained in bulk from oil merchants or through any chemist. A double boiler or steamer is used to melt the wax, the melting-point of which is around 110° F. The receptacle should be of sufficient size to permit the immersion of a hand or foot. When the limb has been immersed the patient should be instructed to keep it perfectly still for a few seconds or the sensation of heat may become unbearable. It is withdrawn and immersed repeatedly, the wax being allowed to solidify on the limb after each immersion, until five or six coats of wax have been applied. The part is then wrapped up in jaconette and cotton-wool for twenty to thirty minutes. The skin perspires freely beneath the wax and a local vapour bath is formed. At the end of the treatment the wax is easily peeled off and leaves an intense erythema of the skin which lasts for some time. The wax can be used again and again. This method is very valuable in the treatment of hands and feet of those affected by rheumatoid arthritis. Pain is eased and movement of the joints is improved. When the affected joint cannot be immersed in the wax (knee, shoulder, etc.), several coats of hot wax are applied by means of a large paint brush, jaconette and cotton-wool being used to retain the heat as before.

**Glove Bath.**—A method devised by Ray for the local application of

heat to the hands or feet has been found to be of service. The hand or foot is covered by a rubber glove or rubber sock several sizes too large and then immersed in water at a temperature of about 110° F. for fifteen to twenty minutes. The skin perspires freely within the rubber covering, pain is relieved and movement improved. The effect of this form of treatment can be enhanced by the application to the limb, before it is covered with the rubber, of oil of wintergreen or iodine.

All the methods outlined can be used in the home and are comparatively cheap. More elaborate procedures are available in the hydrological establishments at the spas, but those described above are equally efficient and the average patient or his friends can readily be taught to use them effectively.

### MANUFACTURE OF PLASTER SPLINTS

**Wrist Splint.**—Soak a plaster-of-Paris bandage 3 yds. long and 4 in. wide in lukewarm water to which a little salt has been added (one to two teaspoonfuls to a basin of water). On a smooth surface (a sheet of thick plate-glass is perhaps the best) make a slab 14 to 16 in. long by rolling the bandage backwards and forwards upon itself. As each successive layer of bandage is added it is rubbed smooth with the palm of the hand in order to get rid of air bubbles. When the slab is complete it is grasped firmly with the finger and thumb about 6 in. from one end and compressed unto a bar (see Fig. 7), which is

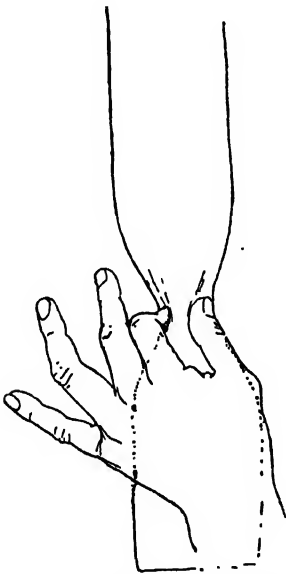


FIG. 7.—Showing how Plaster Slab is Compressed to Form a Bar by the Forefinger and Thumb.

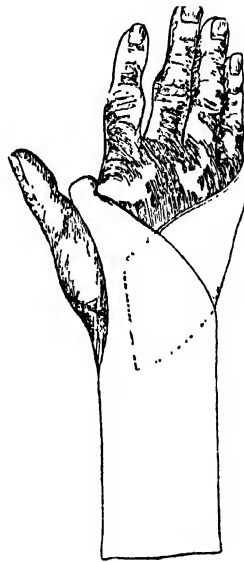


FIG. 8.—Showing the Slab Moulded into Position, short end across the palm and over the dorsum of the hand, long end over dorsum of the hand and up the forearm.

then placed between the first finger and thumb of the patient's hand, the shorter end of the slab being on the palmar aspect. This end is moulded across the patient's palm just proximal to the metacarpophalangeal joints and round on to the dorsal aspect of the hand and wrist. The other end of

the slab is moulded across the dorsum of the hand and up the forearm (see Fig. 8). A plaster bandage is now applied to the forearm and wrist, which

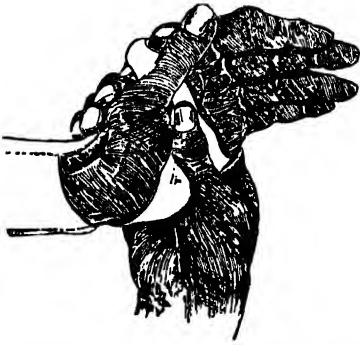


FIG. 9.—Showing how the Splint is Moulded to hold the Wrist in Dorsiflexion. Dotted lines on the anterior aspect of the wrist indicate where plaster is to be cut.

is held slightly in dorsiflexion and the transverse palmar arch maintained by pressure of the operator's thumb (see Fig. 9) until the plaster has firmly set. The plaster on the anterior aspect of the forearm and wrist is now cut away (see Fig. 9) and the splint slipped off. The splint is allowed to dry for twelve hours, after which it can be readily slipped on and off and when in use kept in place by a bandage (preferably crêpe) applied to the forearm. This type of splint is used when the wrist alone is involved. In the acute stage its function is to prevent deformity and secure absolute rest to the joint. In the subacute and chronic stages, where flexion deformity of

the wrist already exists, a series of these plasters may be used for its correction, according to the technique described for the knee (see p. 843).

**Hand and Wrist Splint.**—Make a short slab of plaster bandage 3 to 4 in. wide and 6 to 8 in. long, consisting of six thicknesses of bandage. It is moulded around the fingers and hand. Make a second slab 10 to 12 in. long and 4 in. wide, consisting of six to eight thicknesses of bandage. Apply it along the forearm, hand and fingers, overlapping the first slab (see Fig. 10). The two slabs are now fixed together with a plaster bandage. While the plaster is still soft, ulnar deviation is corrected, the wrist dorsiflexed and the palmar arch restored. When the plaster is firm, the splint is slipped off and trimmed in order to ensure its easy application and removal. When in use it is held in place by a forearm bandage, as shown in Figs. 10 and 11. The splint is used for rest in the acute stage and correction of ulnar deviation and flexion deformity of the wrist in the subacute and chronic stages.

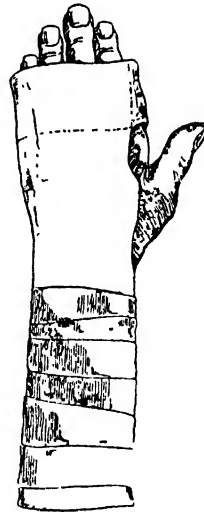


FIG. 10.—Hand and Wrist Splint—Posterior Aspect.

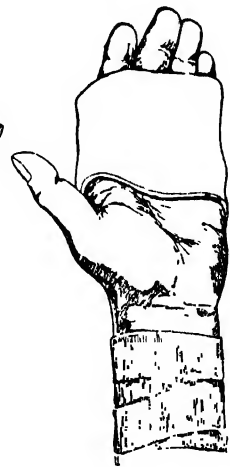


FIG. 11.—Hand and Wrist Splint—Anterior Aspect.

**Rest Splint for Use in the Acute Stage of Rheumatoid Arthritis.**—For the manufacture of this type of splint a mould is required, consisting of a length



FIG. 12.—Aluminium Mould used in Manufacture of Rest Splint for Hand and Wrist.

of aluminium 4 in. wide and about 18 in. long. It is bent at one end so as to form an eminence upon which the hand rests (see Fig. 12).

The mould is covered with a single layer of stockinette and a plaster slab is made and placed upon the mould. The slab should overlap slightly around the edges of the aluminium. The patient's hand and forearm are then pressed on the slab (see Fig. 13) and the stockinette pulled tight over them, the thumb being left free. This has the effect of moulding the plaster firmly to the limb. When the plaster has become set, the splint is removed and trimmed and allowed to dry for twelve hours. When in use it is kept bandaged firmly to the hand and arm with a crêpe bandage.

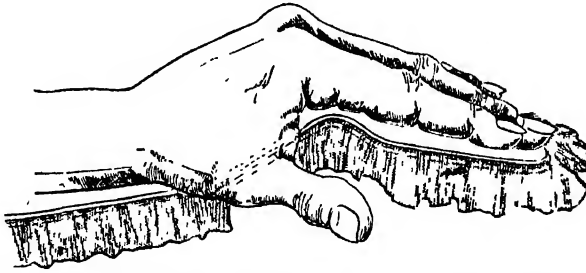


FIG. 13.—The Mould (shown by dotted lines) has been covered with Stockinette. The Hand is resting on the Plaster Slab. The stockinette is used to mould the slab to the hand and wrist as described.

The splints described must be adapted and modified to suit each individual case. The measurements given are approximate, and it is essential that the splint should be as light as is compatible with strength.

**Serial Plasters for the Correction of Flexion Deformity of the Knees.**—The first plaster is applied in the position of deformity to the limb which is encased in stockinette. A plaster slab is made, 4 in. wide and five to six layers of bandage thick, and long enough to extend from the gluteal fold to beyond the toes. It is held in position by an assistant while the first bandage is applied from above downwards. The bandages should be 6 yds. long by 4 in. wide. In order to facilitate the application, the patient's pelvis should be raised on sandbags or a pelvic prop. When two to three bandages are in position the knee should be gently coaxed into the position of maximum extension and the plaster allowed to set. This will allow the limb to be handled more freely without inducing a recurrence of muscular spasm with subsequent loss of extension. A further four or five bandages should be used to complete the plaster, which should extend from the groin to the metatarsophalangeal joints of the toes. The portion of slab extending beyond the toes should be folded back so as to form a sole to the footpiece. Before the last bandage is applied, the stockinette at the upper and lower ends should be folded back on the plaster to cover the edges and prevent chafing of the skin. When the plaster is complete it should be marked with the date and the angle of the knee. On the following day (some workers advise waiting two or three days) the plaster is bivalved (see diagram) so that treatment of the muscles can be resumed. Great care is required in cutting the plaster, as severe pain may be caused by undue pressure over the tender joints and the confidence of the patient may be lost. Considerable experience in the use of plaster shears is required. After the plaster has been cut the splint is kept in position by a bandage or straps, except during treatment to the muscles (see Fig. 14). In five to six days a useful

gain in extension should have occurred and a new plaster must be applied. The limb should not be removed from the first plaster until everything is ready for the application of the next, as spasm tends to return as soon as

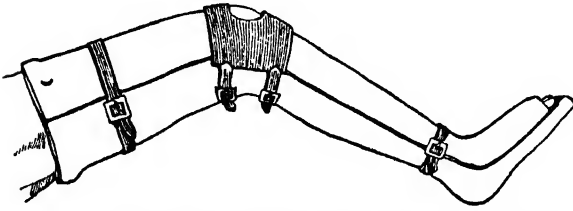


FIG. 14.—Serial Plaster Bivalved and Held in Position by Straps and Kneecap.

the support of the plaster splint is removed and difficulty may be experienced in consolidating what has been gained. The application of five or six serial plasters may be required for the restoration of full extension of the knee. In more obstinate cases a final

manipulation under a general anæsthetic may be required (see p. 822).

**Wedge Plasters.**—The principles underlying this method have already been explained. The only differences in applying the plasters are the incorporation of a short anterior slab over the knee to act as a hinge, and, as a whole, the splint is rather heavier than that employed in the serial technique (see Fig. 15).

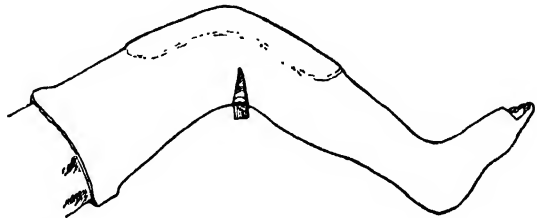


FIG. 15.—Wedge Plaster. Dotted lines show the anterior slab which acts as a hinge.

## POSTURAL, BREATHING AND RE-EDUCATIONAL EXERCISES

### EXERCISES FOR THE ABDOMINAL MUSCLES

**Exercise 1.**—Lying flat on the back with hands at back of neck or on top of head; if the back is hollow in this position, bend the knees. Breathe deeply, raising the chest; do not allow the lower back to lift.



FIG. 16.—Exercise 1: Lying Position.

Hold the chest up and exhale by drawing the lower abdomen in. Take the next breath against the lifted chest; exhale as before, without allowing the chest to drop.

The amount of breath passing is not important; the important points are the constantly lifted chest, which is pushed higher with each breath, and the exhalation by the inward, upward contraction of the lower abdomen.

**Exercise 2.**—Lying flat on back, hands at back of neck, chin in, knees bent. Contract the lower abdominal muscles with an inward, upward pull; tighten the buttock muscles and so flatten the whole back against the floor; relax and repeat. This is not a breathing exercise, but the chest must be held up and the chin in.



FIG. 17.—Exercise 2: Lying Position. The muscle effort is entirely in the pelvic region and low back.

**Exercise 3.**—Same position with bent knees. Bend one knee over the chest, straighten leg and lower slowly, holding chest up, chin in, abdomen in, keeping the back flat on the table. Repeat.

**Exercise 4.**—Lying flat with hands clasped on top of head, elbows back, chin in, back flat. Stretch one whole side; feel a lateral upward spread of the ribs; hold the stretch and slightly contract the lateral abdominal muscle on the same side; relax. Repeat, alternate.

**Exercise 5.**—Lying flat, chin in, chest up, back flat. Grasp ribs at costal margins firmly with both hands, breathe deeply pulling ribs outwards; hold ribs out and exhale by drawing upper abdomen in. Hold the lateral spread of the ribs and inhale again, spreading the ribs farther. Do not relax until the required number of breaths have been taken. The amount of air passing is not important; the lateral spread of the ribs and the increased motion of the diaphragm are the points worked for.

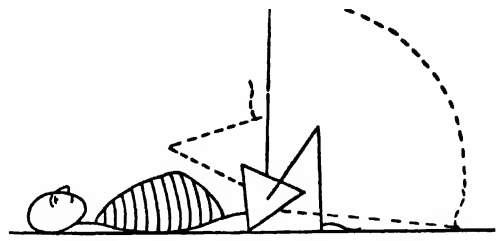


FIG. 18.—Exercise 3: Lying Position.

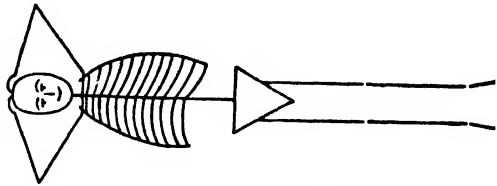


FIG. 19.—Exercise 4: Lying Position. Chest and ribs lifted by lying position. Ribs of one side separated by a muscle pull.

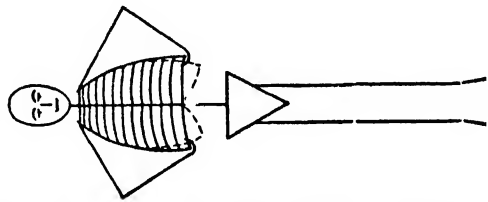


FIG. 20.—Exercise 5: Lying Position. Ribs and chest lifted by lying position. Lateral spread of lower ribs at inhalation.

### ARM, NECK AND SHOULDER EXERCISES

Arm, neck and shoulder exercises in the same lying position are of more value than those done while standing, because the body is in good position without muscular effort and localized exercises may be used to more advantage. In all of the following exercises the most important feature is whether the body, chest, abdomen, spine and head are held in a correct position. This is of much more consequence than the actual movement of the extremities.

**Exercise 1.**—Lying flat, chin in, knees bent if the back hollows, elbows bent and held against the ribs. Extend arms out to the side at shoulder level, palms turned back; return and repeat.

**Exercise 2.**—Same position, extend arms behind head, keeping elbows on body level, palms facing upward, with arms at full extension; return and repeat.

**Exercise 3.**—Same position, chin in. Hold arms extended sideways at shoulder level; rotate shoulders and arms backward. Let the shoulders carry the arms in order to allow the rhomboids to contract.

**Exercise 4.**—Same position, hands at back of neck. Pull chin in, stretching back of neck; relax and repeat. Do not lift the head or shoulders off the table.

**Exercise 5.**—Same position, hold chin in, turn head to side; alternate.

**Exercise 6.**—Same position. Hold chin in, bend head to side, toward the shoulders; alternate.

**Exercise 7.**—Same position, arms straight at sides. Raise arms sideways to back of head, keeping them on body level; stretch whole body upward. Keep chin in and back flat.

### SITTING EXERCISES

Sitting exercises may be undertaken when the lying exercises have been mastered.

The sitting position is preferable to the standing position as the next step in the progression of exercises. The reason is that in the sitting position it is easier to keep the back flat and the abdomen in. The first lateral flexion and rotation should be done in this position because the pelvis and hip joints are locked and the motion is localized in the upper spine.

**Exercise 1.**—Sit straight and tall, abdomen in, back flat, head up and chin in, hands on hips. Breathe deeply, pushing chest up and forward; hold chest up and exhale by drawing lower abdomen in and up; relax and repeat.

**Exercise 2.**—Same position, hands clasped on top of head, elbows back, chin in, head up, chest up and forward. Pull lower abdomen in and up; relax and repeat. Do not hunch shoulders. This is not a breathing exercise.

**Exercise 3.**—Same position. Stretch one whole side, spreading ribs apart, pull abdomen in; alternate. Do not sway or bend the trunk, but simply stretch the whole side.

**Exercise 4.**—Same position, hands on hips. Bend upper part of trunk to side; alternate.

**Exercise 5.**—Same position. Turn upper part of trunk to side; alternate.

**Exercise 6.**—Same position. Tighten buttock muscles; relax and repeat. Hold rest of body in good line.

**Exercise 7.**—Same position, hands clasped on top of head, elbows back, head up, chin in, back flat. Breathe deeply, pulling chest up; hold chest up and exhale by drawing lower abdomen in.

### STANDING EXERCISES

The progression of exercises is usually from lying, to sitting, to standing work. The progression is made from one to the other as soon as the patient has mastered the fundamentals of good body mechanics. The object of the whole series is a well-poised body with the least amount of muscular effort. If the poise becomes rigid or strained, the aim of the exercises has been missed. The effort should be to teach the use of the whole body in good anatomic and mechanical alignment, which means the least amount of muscle work, and therefore the least amount of strain and fatigue.

A good standing position consists of the following: Feet comfortable, straight ahead, with the weight well forward and on the outside borders;

abdomen in, back flat, chest up and forward, head up, chin in, and body relaxed. To relax does not mean to collapse but to balance the weight of the body on the feet like a stick balanced on a finger. With the body in good line, find the balance point and always maintain it. When such a position has been acquired, exercises of any type or theory or "ism" may be done with the greatest amount of benefit as long as they do not force the body into positions of deformity or bad body mechanics.

**Exercise 1.**—Stand against wall, feet 4 to 6 in. away from wall, head, hips and shoulders against wall, chin in; stretch tall, hands at back of neck. Push elbows back, breathe deeply, hold chest up, exhale by drawing lower abdomen in. Do not let the back arch away from the wall.

**Exercise 2.**—Same position, hands on hips. Pull lower abdomen in and up, tighten and pull buttocks down to flatten the back against wall; relax

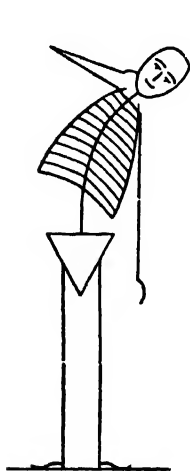


FIG. 21.—Exercise 4: Standing Position. Lateral flexion of dorsal spine. Hips and pelvis fixed. Elbow and head back, chin in.

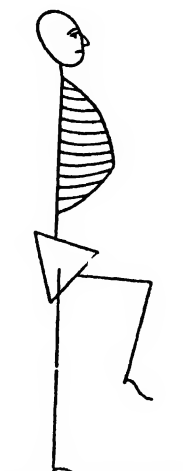


FIG. 22.—Exercise 8: Standing Position. Flexion of the knee and hip. Ribs, chest and head up, back flat.

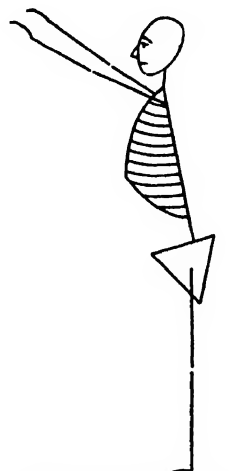


FIG. 23.—Exercise 9: Standing Position. Forward upward lift of arms, chest and ribs, back flat and head up, weight forward.

and repeat. Keep chest up and chin in; do not bend the knees. This is not a breathing exercise.

**Exercise 3.**—Same position; hold abdomen in and chest up. Pull chin in, stretching back of neck; relax and repeat. Do not lift shoulders or let head leave wall.

**Exercise 4.**—Good standing position, feet straight, weight well forward and on outer borders, head up, chin in, chest forward, abdomen in, back flat (Fig. 21). One hand at back of neck, elbow back, other hand on thigh. Bend upper part of trunk to side of lower hand, straighten and repeat. Do not let hips sway.

**Exercise 5.**—Good standing position, feet apart, arms held sideways at shoulder level, palms down, head up, chin in, chest forward, abdomen in, back flat. Bend upper part of trunk to side; alternate. Do not sway at hips or ankle joints.

**Exercise 6.**—Same position. Turn upper part of trunk to side; alternate.



**Exercise 7.**—Good standing position, hands on hips, weight well forward, head up, chin in. Stretch tall. Walk on straight line, make forward heel meet backward toe, toe in slightly.

**Exercise 8.**—Good standing position, hands on hips, stretch tall, head up, chin in, chest forward, abdomen in, back flat (Fig. 22). Bend knees up; alternate. Do not allow the upper part of trunk to sway.

**Exercise 9.**—Good standing position. Inhale, raising arms forward and upward, rise on toes, stretch tall (Fig. 23). Let arms sink to side as heels sink, exhale by drawing lower abdomen in. Keep chest up and forward and back flat.

### FOOT EXERCISES

Exercises to correct faulty body mechanics should always include training in the proper use of the feet. It should be remembered that when a muscle is used in the right way it becomes stronger, and therefore before any foot exercises are given the patient should be shown how to use the feet properly. The correct standing position must begin with the position of the feet in weight bearing. The feet should be comfortably straight ahead with the weight on the outer border, toes on the ground. Use of the feet in this position means correct use of all the foot muscles.

**Exercise 1.**—Sitting, cross knees. Make half circle with foot, down, in and up. The inward, upward pull is the important result.

**Exercise 2.**—Same position, turn foot in slightly. Pull foot up and push down, using ankle joint.

**Exercise 3.**—Same position. Turn foot in, curl toes under hard. Pull foot up when toes are curled.

**Exercise 4.**—Standing, weight well forward, body in good line, hands on hips. Lift inner borders of feet, relax half-way and repeat. Toes cling to floor.

**Exercise 5.**—Same position. Lift inner borders of feet, rock from heel to toe. Do not let inner border of feet down.

**Exercise 6.**—Heel-and-toe walk on line. Described in previous list.

**Exercise 7.**—Sitting. Pick up marbles with toes, turn foot up, and hand to yourself.

**Exercise 8.**—Sitting. Place bath towel, folded full length, on floor; using toes and outer border of foot, draw whole length of the towel towards you. Do not let heel move out of position or rest on towel.<sup>1</sup>

### HAND EXERCISES (*Active*)

**Starting Position.**—Sitting at a table with the forearm at a right angle and supinated to mid-position.

**Exercises to Enable Patient to Flex Fingers.**—1. Flexion of each joint of the fingers separately into the palm of hand, assisted by other hand or operator.

<sup>1</sup> We are greatly indebted to Drs J. E. Goldthwait, L. T. Brown, L. T. Swaim and J. G. Kuhns, the authors of "Body Mechanics in the Study and Treatment of Disease" (J. B. Lippincott & Coy., Philadelphia), for permission to reproduce the text and diagrams of the postural and breathing exercises quoted above.

2. Place a small rubber ball into the palm and tell patient to alternately "squeeze and release." This may be made more difficult by using a soft piece of sponge.

**Exercises to Overcome Flexion Deformity.**—1. Placing the hand as flat as possible on the table and with the forearm fixed stretch the fingers forward as far as possible.

2. Stretching fingers and lifting each up off the table separately.

**Exercises to Obtain Extension of Wrist.**—1.\* Forearm supinated, hand over edge of table, wrist extension.

Same exercise may be performed with gravity eliminated, *i.e.*, with forearm in mid-position; or gravity resisting, *i.e.*, forearm pronated.

2. Place forearm on table, palm downwards; raise forearm up, keeping hand fixed.

3. Wringing a duster.

4. Climbing up the wall bars.

**Exercises to Obtain Flexion of Wrist.**—1. Same as (1\*), except the arm is pronated in the first part of exercise and the wrist is moved to the flexed position.

#### Other Exercises.

1. Stretching the fingers upon the table, separate them as far as possible. If adduction is limited, adduct each finger separately to the middle line of the hand.

2. Forearm supinated, flex the thumb into the palm of the hand.

3. In same position oppose thumb to little finger.

4. With wrists extended and resting on edge of table, perform movements with fingers as if playing piano, taking care not to produce ulnar deviation.

5. Picking up objects (large ones to commence with) such as a reel of cotton with the thumb and each finger separately. This may be progressed by picking up large pins, needles and small pins.

6. Writing with pencil.

#### DETERMINATION OF THE SEDIMENTATION RATE

The test consists of the measurement of the rate of fall of the blood corpuscles in a perpendicular column of blood maintained at room temperature (65° F.). To obtain accurate readings an elaborate technique is required. General practitioners have neither the time nor the apparatus for carrying out such a procedure, but a simple method is available which is sufficiently accurate for practical purposes. Westergren tubes are used, and these can be obtained commercially, mounted on a convenient rack. The tubes are graduated from 0 to 200 mm. The length of the column in millimetres of the supernatant plasma created by the sedimentation of the erythrocytes is noted every half-hour up to two and a half hours. For most purposes the one-hour reading will suffice.

The test is not diagnostic of any particular disease, since an increased sedimentation rate is found in all infections. In a healthy individual the sedimentation rate is 5 mm. or less in an hour. In the acute stage of rheumatoid arthritis the one-hour reading may be 80 to 100 mm. or even more. When the activity abates as a result of treatment, or during a natural remis-

sion of the disease, the rate decreases, but any intercurrent infection such as a common cold or influenza will cause a definite rise. If the test is carried out at regular intervals (once weekly) it serves as a useful guide to the progress of the case and the effect of treatment. In addition, it is of value as a diagnostic procedure, particularly in chronic arthritis, as a normal sedimentation rate favours a diagnosis of a degenerative or traumatic condition (osteo-arthritis) rather than a toxic or infective state (rheumatoid arthritis, focal arthritis, etc.).

**Method.**—Five cubic centimetres of blood are withdrawn from a vein into a dry sterile syringe and immediately ejected into a clean tube containing crystals of potassium oxalate. The amount of anticoagulant required is approximately 2 mg. per cubic centimetre of blood. For 5 c.c. of blood this is roughly the amount which can be conveniently picked up on to the point of a penknife. The blood and anticoagulant must be well mixed by repeatedly inverting the tube. The test should be done as soon as possible after the withdrawal of the blood and certainly within three hours. The Westergren tube is filled by sucking the oxalated blood up to the zero mark and then mounted in the rack provided. Readings are taken at half-hourly intervals, but in most cases the one-hour reading will suffice.

### THE ORGANIZATION OF A RHEUMATISM CLINIC

As has already been emphasized, a prolonged stay in hospital is often essential for the treatment of arthritis, especially of the rheumatoid type. On discharge from hospital the patient has to readjust himself to a mode of existence demanding the assumption of a certain degree of independence and responsibility and too often finds himself unequal to the task. If the best results are to be obtained from institutional treatment, provision must be made for the supervision of such patients on their return to home and occupation. Accordingly an important function of a hospital or clinic for the treatment of chronic rheumatic disease is the provision of a social service department to undertake the care and supervision of patients after their discharge. This service is particularly required for those patients who, for medical or financial reasons, are unable to report at the clinic at regular intervals for medical and orthopædic overhaul. Certain members of the social service department must receive special instruction in the various problems peculiar to the chronic rheumatic diseases. They must visit these patients at regular intervals and report progress to the physician in charge of the case. It is also their duty to improve home conditions where these are unfavourable and to help the patient find employment which will not predispose to exacerbations of the disease (see p. 804 *et seq.*).

It has long been recognized that severe mental shock, profound emotional disturbance and long-continued states of worry and anxiety appear to be of ætiological importance in initiating the onset or precipitating a relapse in patients suffering from rheumatoid arthritis. The psychological aspect is also of importance in patients who, after months or even years in bed, have lost the desire to assume once more the responsibility of independent existence. The correction of this mental attitude is essential and requires the most careful consideration of the medical and social service. It is only by close co-operation and prolonged supervision that the full benefit of treatment can be ensured.

**Occupational Therapy.**—One of the most difficult aspects of the treatment of arthritis of the rheumatoid type is the rehabilitation of the patient once the active stage of the disease has passed. Re-educational exercises, physiotherapy, etc. (see p. 819), may do much to improve movement and muscular tone, but restoration of full function in the affected limbs may be very difficult to obtain. In American clinics, occupational therapy has been used with great success for this purpose. Weaving, using a loom driven by hand or foot controls, basket work, metal work, leather work and painting are examples of the type of work employed. The selection of the occupation is determined by the degree of incapacity present and the particular joints involved. In addition to its therapeutic use in restoring function, occupational therapy provides a psychological stimulus of great value. The patient's interest is aroused and his mental outlook improved. Many patients acquire a high degree of skill, and the sale of articles manufactured may provide a source of income where return to a former occupation is impossible.

## GOUT

Gout is a disease characterized by recurring attacks of acute pain, swelling and inflammation affecting a joint or joints, and by the deposition of sodium biurate in the form of tophi in and around joints, in bursæ and in the cartilage of the ears. The disease is associated with an inherent abnormality of purine metabolism the nature of which is quite unknown. The joint most commonly involved is the metatarso-phalangeal joint of the big toe. Gout is extremely rare in women. In the majority of cases a hereditary factor plays some part. A proportion of cases of fibrositis affecting muscles, tendon sheaths and fascial planes are believed to have a gouty basis. As the disease progresses the condition tends to become chronic and osteoarthritic changes appear in the joints affected. Acute attacks are usually associated with dietetic indiscretion, but may be precipitated by over-exertion, excessive mental strain, injury, exposure to cold, or a surgical operation. They usually occur in the spring or autumn months. The blood uric acid is often elevated at the beginning of an acute attack but may fall to a normal level between-times. In more chronic cases it tends to remain consistently above normal (normal value 3 to 4 mg. per 100 c.c.). There is, however, no constant relationship between the serum uric acid concentration and the frequency of attacks or the severity of the clinical features. The acute attacks are often preceded by symptoms of dyspepsia or mental depression and irritability.

**Treatment of Acute Stage.**—Because of the pain, malaise and slight fever, the patient is best confined to bed. The bowels should be opened by the administration of 1 to 2 gr. (0.06 to 0.12 gm.) of calomel or a blue pill at night, followed next morning by a saline purgative.

By far the most effective drug for the relief of the acute attack is colchicum, which when properly administered may be expected to ensure relief within twenty-four to seventy-two hours. How the drug accomplishes this effect is quite unknown. It neither lowers the serum level of uric acid nor increases its excretion. In Great Britain it is the custom to prescribe colchicum in the form of 15 minims (0.87 c.c.) of the wine together with 20 gr. (1.2 gm.) of sodium salicylate and 20 gr. (1.2 gm.) of potassium bicarbonate, the mixture to be taken every two to three hours for the first

twelve hours and thereafter three or four times daily until the acute symptoms have subsided. Leading American authorities (Hench, Bauer and Klemperer, 1944) state that most consistent and effective results are produced if the drug is prescribed in the form of crystalline colchicine since tinctures and wines are notoriously unstable preparations and variable in their content of the active principle. They recommend that colchicine be prescribed in the form of pills or capsules each containing half a milligramme (gr.  $\frac{1}{120}$ ) of the alkaloid. The initial dose recommended is one milligramme followed at two-hourly intervals by half a milligramme until relief of pain is obtained or vomiting or diarrhoea result. Provided the patient is kept in bed, pain should be relieved within twenty-four to seventy-two hours after the institution of treatment. The total amount of colchicine to relieve the acute attack varies from case to case, but in general is somewhere between 4 and 8 milligrammes. In some cases the gastro-intestinal symptoms may be so severe as to require treatment with camphorated tincture of opium in doses of 60 minims (3.48 c.c.) after each loose motion. In the treatment of subsequent acute attacks of gout the total amount of colchicine prescribed should be one or two milligrammes less than that quantity found to produce severe diarrhoea. So successful may this method be that it is recommended that patients should always carry with them a supply of colchicine pills which should immediately be taken in the way recommended above, on the appearance of prodromal symptoms or the first twinge of articular pain. By this means it is claimed that patients may be spared prolonged and incapacitating seizures. This method of treatment is not entirely without danger. In one case in the authors' experience a patient collapsed and died after a total intake of 7 mg. of colchicine. Such a catastrophe must be considered as due to an individual idiosyncrasy to the drug, but emphasizes the need for careful observation of the patient when the drug is administered for the first time.

Heat should be applied to the inflamed joint in the form of a kaolin poultice, and the pressure of the bedclothes avoided by means of a cradle. A lacto-vegetarian type of diet should be prescribed. Purine-containing foods must be reduced to a minimum. The total calories in the diet should be around 1,500, the reduction being obtained at the expense of protein and fat. Fluids should be taken freely, 4 to 5 pints being drunk daily. A glass of hot water containing 20 to 30 gr. (1.2 to 1.8 gm.) magnesium sulphate or a glass of Vichy water taken first thing in the morning and last thing at night is of particular value. The diet should be constructed from the following foods which are low in purines or purine-free. Milk, cheese, butter, sugar, jam and fruit are purine-free, while bread, cereals, root and green vegetables, tripe and eggs contain less than 0.06 gm. purine nitrogen per 100 gm., and can be considered foods low in purine. Tea, coffee, cocoa and meat extracts must be avoided, since they are beverages rich in purines. Alcohol should be completely forbidden during an acute attack. If the pain is severe, analgesics are necessary. A tablet containing aspirin, phenacetin and codeine may be sufficient, but occasionally even morphia may be required. Under this régime the acute symptoms are usually controlled in a few days.

**Treatment between Attacks.**—When the acute attack has subsided, careful attention must be devoted to the patient's general mode of life. Our ignorance of the ætiology of gout, the variability in the duration of freedom

from attacks in different persons and in the same person from time to time and the absence of any satisfactory yardstick, including estimation of the serum uric acid concentration, by which the value of preventive measures can be ascertained, are factors which make it extremely difficult to give sound advice on the treatment between attacks. Generations of physicians in Great Britain have laid emphasis on the value of dietetic treatment. Recent metabolic and experimental studies in America carried out by Bauer and Klemperer (1944) throw considerable doubt on these claims which are based mainly on clinical impressions. These writers state that from a careful review of the literature they are unable to find satisfactory evidence that dietary treatment influences the clinical course of gout. They were unable to provoke or prevent attacks by giving or withholding food rich in fat or purines or alcohol. We do not feel justified at the present time in entirely accepting these conclusions, but submit that the degree of dietary restrictions recommended must be assessed by trial and error in each individual case.

*Diet.*—Uric acid in the blood and tissues comes from two sources: endogenous from the breaking down of the body tissues; exogenous from the nucleoproteins contained in the food ingested. Endogenous purine metabolism can be lessened to a limited extent by a reduction in protein intake and of the total caloric value of the diet. Purines from exogenous sources can be curtailed at will by dietetic measures. Therefore the diet in chronic gout is based on three principles: (1) low caloric value; (2) reduced protein and fat intake; (3) low purine intake. While the general principle must be maintained that foods rich in purines should be curtailed, due consideration must be given to the fact that we are dealing with a disease which will persist throughout the patient's life, and a more varied type of diet than that employed in the acute attack must be allowed. The degree of dietetic restriction must be regulated in each individual patient according to the frequency with which the attacks occur and their severity. The following articles should be excluded permanently because of their high purine content: Fish-roe, sweetbreads, whitebait, sprats, sardines, heart, venison, herring, mussels, liver, goose, kidney, bloaters. A moderate helping of meat, white or red, should be allowed at one meal during the day, and an average portion of fish or chicken at night. It must be noted, however, that the purine content of white fish, sole, haddock and cod is as high as that of chicken or beef. Fish with a high fat content, such as salmon, are generally forbidden, but their purine content is approximately the same as white fish, meat or chicken, while their protein content is lower. Their exclusion can only be justified, therefore, owing to a personal idiosyncrasy or because of their fat content. Plenty of green vegetables and fruit, fresh or stewed, should be taken. If the patient is sensitive to any particular variety, it should be prohibited. Strawberries, spinach and rhubarb are generally prohibited because of their tendency to cause oxaluria. Cereals, milk, cheese, eggs, sugar, jam and honey need not be restricted since they are foods low in or free from purines. Since some evidence exists that the ability of the serum to dissolve sodium biurate is reduced by sodium salts, it has been suggested that sodium chloride should be used sparingly both in cooking and at the table. It seems unlikely to the authors that the small amount of salt used could affect the level of sodium ions in the blood. In those cases where the gouty tendency is marked, all forms of alcohol should be forbidden. In less severe cases the heavy wines such as burgundy and port should not

be indulged in, but a glass of claret or Moselle may be allowed on occasions. A little whisky, well diluted with water, may be taken without harmful results, but beer is best avoided. If the patient is overweight, it is extremely important that the weight should be reduced, due respect being given to the principle of limiting the purine-rich foods in the anti-obesity diet prescribed.

*Drugs.*—The effect of cinchophen in promoting the excretion of uric acid is well recognized, but its administration is not altogether without danger. In patients sensitive to the drug, toxic reactions may occur, usually in the form of a hepatitis. The danger of toxic reactions has been probably overstressed. If the drug is withheld from elderly patients with cardiovascular or renal disease and from individuals who give a history of hepatitis or jaundice, cinchophen can safely be employed, provided the measures mentioned below are carried out. It is best reserved for those cases in which the gouty state has become chronic and where the blood uric acid remains consistently high despite dietetic treatment and the general regulation of the patient's life. Such patients may derive considerable benefit from a periodic course of cinchophen. The drug is prescribed in  $7\frac{1}{2}$ -gr. (0.45 gm.) doses thrice daily for a period of three to four days, then stopped for a week. The simultaneous administration of alkalis is said to diminish the irritating effects of the drug on the stomach. Cinchophen should be discontinued when the blood uric acid approaches a normal level. Cinchophen, when given to selected cases on the above lines, may be of great value in diminishing the number of acute exacerbations.

Bauer and Klemperer's metabolic studies have shown that sodium salicylate and acetylsalicylic acid are as effective as cinchophen in promoting the excretion of uric acid and hence are the drugs of choice for this purpose since they do not possess the toxic properties of cinchophen. The dose of sodium salicylate is 100 to 120 gr. (6 to 7.2 gm.), and of acetylsalicylic acid 60 to 70 gr. (3.6 to 4.2 gm.) in divided doses daily; alkali should be prescribed with each dose. It has been the custom in the past to prescribe salicylate for three-day periods in each week, but Bauer and Klemperer have shown that the increased excretion of uric acid resulting is followed by an increased retention so that the total amount excreted over a period of seven days is insignificant. Accordingly they recommend that when attacks of gout are occurring rapidly at short intervals salicylate in the doses suggested above should be given daily for a month, by which time the concentration of serum uric acid will be reduced to one-third of the pre-treatment level, and its return to the original level will be delayed for several weeks.

*General Management.*—Exercise in moderation is of undoubted value in the treatment of chronic gout, but over-exertion may precipitate an acute exacerbation. Plenty of fluids should be taken. The daily use of purgatives should be avoided, but an occasional dose of calomel at night followed by a saline laxative the next morning is often of value to the plethoric patient. Clothing must be warm, and the patient should be warned against undue exposure to cold and damp. A daily warm bath followed by a brisk rub down improves the tone of the peripheral circulation and promotes diaphoresis. Sufferers from chronic gout derive great benefit from an annual visit to a spa, where general treatment takes the form of vapour, hot air and immersion baths, while the spa waters, taken internally, have a mild diuretic and laxative effect. Mud packs applied to the liver are said to

stimulate its activity. Local treatment to the joints in the form of mud and peat packs, wax baths and the other forms of physiotherapy described on pp. 819 to 821 do much to reduce pain and stiffness. The relief obtained by taking an annual "cure" at a spa is well substantiated in cases of chronic gout, but this form of treatment is best avoided during acute exacerbations. The British spas provide excellent facilities for the treatment of gouty patients, and their waters are as efficacious as those of the more fashionable Continental resorts.

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# DISEASES OF BONE

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## HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY

**T**HIS condition occurs secondarily in chronic diseases of the heart and lungs, and rarely in long-continued toxæmic estates. The terminal phalanges of the fingers and toes become enlarged, giving rise to "clubbing." In the more advanced forms of the disease the bones of the hands, feet, forearms and legs may show thickening. Osteo-arthritic changes may appear in neighbouring joints.

The treatment is that of the primary disease. Should the joints of the hand and feet become painful on account of the osteo-arthritic changes, applications of heat in one or other of its forms may have a palliative effect.

## ACHONDROPLASIA

This disease arises during foetal life and affects bones which develop from cartilage. The long bones, skull and pelvis are commonly involved. Growth is stunted, but although deformed the bones are strongly laid down and there is no impairment of general health.

Apart from the necessity for Cæsarean section in female achondroplasiacs who become pregnant, no treatment is required.

## OSTEITIS DEFORMANS

This disease was first described by Sir James Paget in 1877 and is commonly called Paget's disease. Symptoms rarely appear before middle life. The changes in the bones are those of a rarefying osteitis with new bone formation under the periosteum, giving rise to thickening. There is a progressive enlargement of the circumference of the skull, and the long bones become bowed and thickened. The blood phosphatase is raised.

Although calcium, parathyroid extract and vitamin D have been recommended by various authorities, there is little evidence that any line of treatment exercises an appreciable effect on the course of the disease.

## LEONTIASIS OSSEA

This is a descriptive term applied to overgrowth of some or all of the bones of the skull. The cause is unknown and no treatment has been found to have any effect.

## OSTEOGENESIS IMPERFECTA

*(Fragilitas ossium)*

This is a rare condition in which multiple fractures occur during intrauterine life. The foetus is often born dead. In those which survive the bones are excessively brittle and frequent fractures occur.

Treatment consists of protection from injury and careful surgical treatment of fractures when they occur. Phosphorus internally has been advised.

**RICKETS**

See section of Deficiency Diseases (p. 406).

**OSTEOMALACIA**

(*Mollities ossium*)

This disease is now believed to be a form of rickets affecting adults  
See p. 414.

**OSTEITIS FIBROSA CYSTICA**

(*von Recklinghausen's Disease*)

This condition is due to tumour or hypertrophy of the parathyroid glands, and is dealt with in the appropriate section (see p. 435).

**OXYCEPHALY**

In this condition, as a result of premature junction of certain of the cranial sutures, the anteroposterior diameter of the skull is shortened and the height of the vault is greatly increased to provide space for the growing brain. The deformity is usually present at birth. Increased intracranial pressure occurs, giving rise to exophthalmos and eventually to optic atrophy.

Analgesics are required for the relief of headaches. When the signs of intracranial pressure become marked, decompression is advisable.

**MULTIPLE MYELOMA**

(*Myelomatosis: Kahler's Disease*)

In this rare condition there is a diffuse new growth of a sarcomatous nature involving the bone marrow. The bones become softened and spontaneous fractures are common. Anæmia and progressive cachexia occur. The urine of about half the cases contains Bence-Jones protein, which is precipitated on heating the urine to 50° C., dissolves on boiling, and reappears on cooling.

X-ray treatment to bones may alleviate pain, but does nothing to retard the course of the disease. Death usually occurs in about two years.

**OSTEOMYELITIS**

Up to the present time the treatment of this disease has been a surgical problem, but the introduction of penicillin has revolutionized treatment. For details see p. 94.

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# DISEASES OF THE NERVOUS SYSTEM

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## INTRODUCTION

**T**REATMENT of organic nervous disease is a double challenge; the one to the resource of the physician and the other to the conscience of the community. The doctor's problem goes far beyond the mere administration of drugs: he may have to rely on physical and educational forms of therapy, and he must often depute active treatment to others. The problem for the community is an obligation to provide for those who need constant care and to find employment for those who can work, no matter how limited their capacity.

Treatment begins with the doctor's first question to the patient, even before any attempt at diagnosis. Careful history taking and thorough examination are an essential part of treatment: they establish mutual confidence and understanding as a foundation upon which to build effective and rational treatment. With the formation of an opinion, the appropriate pill, powder or potion is prescribed, in accordance with the physician's knowledge and experience of the condition. The actual medicine may be specific or symptomatic in its action; it may cure some reversible process in the nervous system, or merely relieve distress arising from an intractable cause. But such treatment is almost automatic and scarcely touches the human problem in nervous disease. The necessity for wise psychological handling is not exceeded in any other branch of medicine. Bizarre ideas of the function and form of the nervous system give rise to fantastic fears whenever there is a threat to the integrity of that system. Such fears breed symptoms of no organic significance and yet may constitute the main problem in treatment. To weed out this rank overgrowth of fear and anxiety and to prevent the seeding of doubt and apprehension, strenuous effort in several directions is needed. Early confidence on the part of the patient is essential: anything which will mitigate symptoms of organic origin must be prescribed: and the patient must be given a rational account of himself. If no satisfactory explanation of symptoms is given to the patient, the condition remains a mystery to him and anxiety is the child of mystery.

Discretion and judgment must colour pronouncements. The whole truth cannot be revealed to many patients; they must have, nevertheless, a statement which satisfies their reason, or be assured that the physician understands and is neither alarmed nor surprised by the course of events. There is no standard pattern for the explanation; how much or how little is told depends on the nature of the disease, the intelligence of the patient and the personality of the doctor. The use of technical terms and the naming of a definite diagnosis in progressive disease with unfavourable prognosis should be avoided. On the other hand, it is often expedient to

define and delimit a nervous lesion to an intelligent patient by giving the whole explanation of a static or regressive condition. Thus apprehension can be cut short and adaptation encouraged. When the basic clinical picture, shorn of its psychological overlay, is emerging, adaptation to disability is going on at the same time. Natural adaptation is characteristic of the resilience of the patient and may go a long way to the achievement of an excellent final result. Most people, however, require help and guidance. They must be told how much activity can be reasonably expected of them in the face of disability and without prejudice to health. When the invalid is capable of employment it should be the pleasure and not the task of the physician to give particulars of the industrial potential of the patient to employer, social worker or resettlement officer. The goal of treatment is achieved when, in spite of pain or paralysis, a man has regained his self-respect and freed himself from the frustration of illness by being happily and remuneratively employed in work within his capacity.

Ultimate treatment is the responsibility of the community. A growing sense of duty makes suitable employment increasingly available for the nervously disabled. Still, the present outlook for many employable and yet disabled people is far from ideal. The profession has its part to play in putting forward the case for further facilities in industry. Economically the objection is raised that such ventures are unsound. Arguments of this kind can be countered with the fact that many injured and diseased folk, in virtue of their very disablement, work well and steadily to compensate for their inferiority. At times they surpass in output those with every faculty. The disabled person, however, must be given a job he can do well. For some types of disability it is better to segregate the group into sheltered workshops. Some may be employed fully in industry along with normal people, but then the resettled person must have the physical and mental resource to equal the performance of his normal workmate. Working men may suffer an inferior performance from a disabled mate for a short time, but, if the output of the group is interfered with, sooner or later the offender is an outcast.

The provision of vocational training is a welcome sign of a deeper understanding of the problems which afflict the disabled. Often a man can be given such training at the expense of the public to fit him for employment when disease or injury has rendered him incapable of following his former occupation.

The finding of suitable employment is not the only concern of the community. Institutional care is the only ideal solution to many problems of advanced nervous disease. Care at home, demanding the whole-time attention of a relative, is unsound economically and is inferior to that which institutional life can offer. Yet the present position is far from adequate and has had to take second place to the extension of health services for tuberculosis and long-term illnesses with more favourable outlook.

Little has been said about the more acute forms of nervous disorder. These will be considered under appropriate headings because generalizations are scarcely possible. An attempt has been made to lay down certain broad principles for the care and treatment of the great majority of those afflicted with nervous disorder.

## INFECTIONS

### OSTEOMYELITIS OF THE SKULL

The justification for dealing with osteomyelitis is almost self-evident although the problem is surgical: osteomyelitic infection is the precursor of many a severe meningitis or encephalitis. No septic process in the neighbourhood of the nervous system should be allowed to assume dangerous proportions without the most strenuous surgical treatment or chemotherapy. If treatment of those potentially dangerous and threatening lesions is sufficiently energetic, much major intracranial sepsis will be averted. Infected bone must be removed and extra-dural pus drained because the most assiduous treatment with modern drugs cannot cope with such advanced infection. In the case of infection of accessory air sinuses, the advent of penicillin has obviated some of the radical surgical procedures of former times. For example, spread of infection from the ethmoid cells, giving rise to orbital cellulitis, with proptosis, can be overcome without surgical intervention, if taken early enough. Prompt, energetic treatment can avert the disaster of cavernous sinus thrombosis or of generalized meningitis. Protean infections of this kind demand penicillin in full dosage intramuscularly, 300,000 units every three hours. It is usual to combine penicillin treatment with sulphonamide treatment, giving an initial dose of 2 gm. sulphadiazine followed by 1 gm. three-hourly. Therapy should be maintained at this level until after the fever has subsided and symptoms have disappeared. The not-infrequent fault is to stop treatment too soon, with disastrous results and less effective ultimate therapy.

### MENINGEAL INFECTION

The treatment of cerebrospinal fever has been dealt with elsewhere (see p. 11). The same general principles apply to the care of all meningeal infections. With the notable exception of tuberculous meningitis, most types respond to penicillin and chemotherapy.

The attack on the infection must depend on its origin. Continued treatment by penicillin and sulphonamides may be of no avail when the primary focus of infection in the accessory nasal or ear sinuses has been left without surgical treatment.

Systemic treatment, as defined above, in the treatment of osteomyelitis, should be given in meningitis. There are other ways of launching an assault on the infective agent in meningitis. Penicillin, given intrathecally, at once raises the concentration of the drug in the cerebrospinal fluid, attacks the organism in the medium in which it is being cultured and prevents the spread of its ravages to increasing depths of the neural parenchyma. 20,000 units are injected intrathecally, twice daily. The technique is to perform lumbar puncture, drain off cerebrospinal fluid until the pressure has fallen to normal, fix the syringe to the lumbar puncture needle, dilute the penicillin with cerebrospinal fluid and inject. With 2 c.c. containing 20,000 units penicillin, 8 c.c. of cerebrospinal fluid are withdrawn into the syringe before injecting the drug. In spite of systemic and intrathecal administration of penicillin, the clinical picture may deteriorate. Progression of symptoms may be due to the nature of the infective agent or to the formation

of loculi of infection untouched by the drug. With such deterioration intraventricular penicillin is indicated. The dose is the same as intrathecal penicillin and it is also given twice daily. Administration of penicillin by the intraventricular route is a matter for the neuro-surgeon. A catheter introduced into a lateral ventricle is allowed to remain in position as long as intraventricular penicillin is needed. This mode of exhibition is often thought of too late. Its very effectiveness is not an unmixed blessing. Advanced disease with decerebrate rigidity of some duration may be arrested, but the decerebrate state remains because of the irreversibility of the pathological process. Such cases lie for some weeks in a vegetative state as a reproach to the physician for his delay.

**Late Complications of Meningitis.**—Blindness or deafness following meningitis cannot be treated effectively, because of irreversible pathology. The only aid which can be given to the unfortunates is to help them adapt their lives to disaster. They should be encouraged to work within their own resources: for them, special training and employment are available. Mental defect may require segregation and special institutional care. Uncomplicated hemiplegia is consistent with useful employment; dysphasia may require special encouragement and help from the speech therapist when there is enough residual function upon which to build. Epileptic phenomena have to be controlled by anticonvulsant drugs in the same way as seizures due to other causes (see p. 875).

Hydrocephalus, as an acute manifestation of meningitis, usually subsides when the infection is overcome. Adhesive arachnoiditis, however, may cause progressive hydrocephalus. Depending upon the march of symptoms, the hydrocephalic may have to be relieved by removing arachnoid adhesions in the posterior fossa or by other surgical measures to re-establish circulation of the cerebrospinal fluid.

The circulation of the fluid in hydrocephalus of many years' standing has adapted itself to residual pathology and does not call for special treatment; indeed, meddlesome interference upsets the acquired balance and often leads to disaster.

### ENCEPHALITIS

**Acute Suppurative Encephalitis (Brain Abscess).**—The treatment of circumscribed collections of pus within cerebral tissue is neuro-surgical. Drainage is required and any primary focus of infection should be dealt with by the appropriate specialist surgeon. When complete excision of the abscess is possible without loss of important cerebral function, this operation is the one of choice. Infected scar tissue is a source of potential danger; infection may be so locked up within the brain that no symptoms declare themselves, perhaps for years. During the process of surgical treatment systemic penicillin usually prevents such complications as generalized meningitis and venous sinus thrombosis. The treatment of complications from cerebral abscess—epilepsy, dysphasia, hemiplegia—are discussed elsewhere.

It is to be remembered that brain abscesses may be metastatic and not due to spread from septic processes in the immediate vicinity of the brain. The most common cause of such metastatic abscesses is bronchiectasis. Often the abscess is single; modern surgery and chemotherapy permit a direct attack on the abscess and ultimate excision of the process is frequently

possible. The general rules for the treatment of bronchiectasis should be observed (see p. 745).

**Acute Non-suppurative Encephalitis.**—Encephalitides have assumed epidemic proportions from time to time. Indeed, from 1918-1923, encephalitis lethargica was pandemic, and although this diagnosis should rarely be made now, the physician must be prepared to undertake care of a sporadic case of virus encephalitis, or of an encephalitis complicating a specific fever. There is no known specific for any virus encephalitis. Treatment must deal with individual symptoms. Special consideration may have to be given to coping with delirium and restlessness, particularly at night. Sedatives are indicated and large doses may be required. Four to six drachms of paraldehyde can be given rectally, if restlessness and delirium demand it. Care must be taken, however, not to administer hypnotics in excess and cloud the clinical picture. Fluid and salt balance must be preserved, particularly if sweating and vomiting are excessive. Nourishment has to be maintained in spite of delirium and stupor. If necessary, recourse must be had to nasal feeding. For headache it is unwise to use morphine; not merely does this drug obscure the clinical signs, but it tends to increase cerebral congestion. Pain can be relieved by codeine administered hypodermically in doses of  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) repeated at three-hourly intervals.

**Chronic Encephalitis.**—The residual effects of acute virus encephalitis present a problem both to the physician and the community. Mental defect and motor disability defying all attempts at therapeutic control can be dealt with only by institutional care. The great majority of cases of post-encephalitic Parkinsonism have sufficient mobility and mental acumen to fit them for life at home. Many are employable, but the nature of their motor disability imposes limits on their industrial potential. It is quite possible for a comparatively disabled person, slow and tremulous in his movements and indistinct in his speech, to occupy a position of administrative responsibility, when the encephalitic process has left his mentality unclouded. Indeed, some such people have achieved enormous success, because of that compensating drive born of their frustrations. Many are not endowed originally with these qualities of mind to make them efficient administrators; they can frequently be employed as time-keepers or storemen under protected conditions, but seldom are they able to return to their former skilled manual occupations. All encouragement must be given to these sufferers by finding them some form of employment. Those who are mentally clear and capable have to be assured that, even although their motor activity is limited, their minds are lucid and there is no threat to reason. The post-encephalitic has to be advised against employment in cold surroundings. Cold induces increase of muscular tone, the precursor of shivering. That increase of tone is superimposed on the basic muscular rigidity of the condition and adds greatly to the habitual discomfort, constant tremor and limitation of movement. Anxiety and unpleasant emotion in normal circumstances increase muscular tone. The patient should be protected, in so far as possible, against excitement and anxiety.

Physiotherapy is of doubtful value. The exponents of massage claim that effleurage is soothing treatment and lessens rigidity. There is no doubt that this form of massage exerts any value it may have through psychological suggestion. Relaxation therapy may help a little, but all these measures must take second place to the successful adaptation of the indi-

vidual to the restricted life of an irksome disease. Frequent change of posture and passive manipulation of the limbs through their full range of movement afford great relief to the tedium of fixity, but this service does not require the skill of a trained physiotherapist. In spite of the above treatment, certain cases deteriorate; indeed, the encephalitic process may be reactivated and no specific can stop it, so that institutional care may be the only possible final solution.

Drugs which have some effect on the symptoms of post-encephalitic Parkinsonism belong to the belladonna group. They may be exhibited individually, or in combination with one another. Starting with the tincture of stramonium, 20 minims (1.2 c.c.), thrice daily, the dose should be increased gradually to the limit of tolerance, which is usually in the neighbourhood of 4 drachms (14 c.c.) a day. The drug may be combined with hyoscine hydrobromide,  $\frac{1}{160}$ th of a grain (0.4 mg.), thrice daily. Belladonna prescribed in the form of the tincture is of great value in combating hypersalivation, which is often one of the most irksome symptoms. Toxic symptoms such as mental confusion and gastro-intestinal disturbance, necessitate intermission of treatment. Paralysis of accommodation, with dimness of vision, is not an indication for suspending treatment but should be countered by instilling one drop of  $\frac{1}{4}$  per cent. eserine in aqueous solution into each eye daily. Oculogyric crises seem to be induced by psychological stress and are helped by blunting the edge of self-criticism through administration of a small dose of phenobarbitone, daily. Many patients complain of being wakeful at night and drowsy during the day, even in the chronic stages of the disease. For them, chloral hydrate in 20 to 30 gr. (1.2 to 1.8 gm.) doses one hour before retiring is a safe hypnotic. In the early morning, 10 mg. of amphetamine will induce a higher level of activity; this dose is repeated three or four times in the course of the day, but none should be given after four o'clock in the afternoon. Not merely does amphetamine have the effect of preventing narcoleptic incidents, but it may reduce the frequency of oculogyric crises.

Narcolepsy may arise from other causes, but the great majority of cases have had encephalitis. This symptom may be the only sign of the infection. The treatment is amphetamine in 5 to 10 mg. doses, three or four times a day before evening. The narcoleptic cannot be trusted with the safety of others and his employment is therefore restricted.

#### CHOREA (Rheumatic or Sydenham's)

Most cases occur in children and are moderate in severity. The average case needs rest, mild sedation, isolation and the administration of certain drugs reputed to have a specific effect. The child should be nursed in bed in a darkened room for a month, away from noise and bustle. He should receive no visitors; reading and listening to radio are prohibited. Acetylsalicylic acid can be administered in 10 to 15 gr. (0.6 to 0.9 gm.) doses, thrice daily, in the form of aspirin or calcium aspirin. Such a dose is well tolerated by the child of 12 years.

Excessive movement requires the protection of a padded cot bed. Violent and continuous movements may break the surface of skin, especially over the bony points. Friction can be reduced by suitable padding and fixing the pads in position by adhesive strapping.



To give the patient some rest, chloral and barbiturate may be successfully combined as follows:

R	Chloral. Hydr.	.	.	.	.	gr. 10 (0.6 gm.)
	Phenobarb. Sod.	.	.	.	.	gr. $\frac{1}{2}$ (0.03 gm.)
	Syr. Aurant.	.	.	.	.	℥ 30 (1.7 c.c.)
	Aq.	.	.	.	to	fl. oz. $\frac{1}{2}$ (14.2 c.c.)

The mixture may be given two to four times within twenty-four hours, according to the severity of the exhaustion. In more violent chorea, sedatives have to be injected. Sodium phenobarbitone in 2 to 3 gr. (0.12 to 0.18 gm.) doses may be used as an intramuscular injection. Ampoules containing 3 grains (0.18 gm.) are available. When swallowing is impossible, nasal and rectal feeding may be the only methods of maintaining nutrition. Any prolonged case of chorea must have an adequate diet providing readily available energy and, at the same time, make up for the fluid loss of sweating. In severe cases care must be taken to see that the chloride loss of sweating is compensated for by adequate salt in the diet.

The subject of chorea must be watched after treatment has abolished all abnormal movement. He is potentially a sufferer from other manifestations of rheumatism and, accordingly, requires treatment and observation, though it is true that rheumatic carditis is a much less common sequel to chorea than to rheumatic fever.

Chorea insaniens and chorea gravidarum are merely variants of rheumatic chorea and demand the same general regimen in treatment. The violence and mental aberration of these disorders can be coped with only by much heavier sedation than that indicated above.

### INFECTIVE PROCESSES INVOLVING SPINAL CORD

**Suppurative Processes.**—Because of the relatively small mass of the spinal cord, metastatic suppuration within its substance is relatively rare compared with the same process in the brain. Adjacent septic foci seldom extend to the spinal medulla. Infection of vertebrae, however, may give rise to extra-dural abscess, which demands urgent surgical attention—decompression of the spinal cord by laminectomy and flushing the extra-dural space with penicillin. General treatment is the same as in meningitis. Paraplegia requires the same attention as that arising from any other acute cause. (See below.)

Lepto-meningitis may follow extra-dural abscess at any segment of the cord; it rapidly spreads to become general and its treatment is that of generalized meningitis.

**Acute Myelitis.**—This condition is usually of virus origin and there is no specific treatment. The resultant paraplegia requires skilled nursing, particularly when incontinence of urine and faeces complicates the picture. Pressure points must be carefully watched. Neglect of anæsthetic skin causes rapidly developing bed-sores, which become infected and threaten life. The skin must be kept dry, rubbed with spirit and dusted with powder. Posture must be changed frequently. The use of elastoplast for bed-sores is a great advance in treatment. The ulcer is covered and discharges are allowed to gather. The elastic adhesive plaster should be applied, overlapping the edges and unstretched across the defect, no matter how big

the sore may be; it should be renewed as soon as discharges escape from the edges of the dressing. When the dressing is removed the base of the ulcer is washed with hydrogen-peroxide solution and loose sloughs are removed. The edges of the wound must be thoroughly cleansed and dried before re-application of the elastic adhesive. Care should be taken to pad the region around the sore so that pressure is taken by comparatively healthy tissue. This can be achieved by cotton-wool rings or air cushions. The mattress should be soft in all cases whenever there is threat to the skin; the sorbo-rubber type of mattress is the one of choice. Bed-sores develop very much more quickly in dehydrated, ill-nourished subjects, and care must be taken to maintain the chloride-water balance.

If distension of the bladder is allowed to persist, infection of the urinary tract follows, with prejudice to the future, even when the lesion is reversible. With scrupulous aseptic precautions, the bladder should be catheterized. The repetition of catheterization, twice daily, may suffice to tide the patient over the original insult to bladder innervation. If there be little likelihood of early recovery of the bladder, recourse may be had to an indwelling catheter, suprapubic cystostomy or tidal drainage. Preference for suprapubic cystostomy is finding increasing favour. With an indwelling catheter or suprapubic cystostomy, sulphonamides are given to prevent infection ( $\frac{1}{2}$  gm. of sulphathiazole, twice daily, with copious fluids to drink—5 pints per day). In tidal drainage, a weak solution of potassium permanganate keeps the urine clear of infection.

Bowel distension, particularly in the early phases of paraplegia, is troublesome to the patient and a cause of anxiety to the physician. High enemata may be ineffective because of bowel atony, but, nevertheless, should be given a trial first. Much help can be obtained in more obstinate cases by the use of parasympatheticomimetic drugs, after all faecal material has been removed digitally from the rectum (Prostigmine—1 mg. initially, and 0.5 mg., four-hourly). Although this drug relieves abdominal distension, it should be remembered that the flatus tube is often an effective instrument and that prostigmine does cause faintness.

After acute myelitis, complete recovery is possible. The disease, however, may be so extensive that the greatest care cannot avert a fatal issue. Between these extremes, all degrees of disability occur. The bedridden, incontinent patient requires hospital care; those with sufficient mobility merit employment under the conditions of the protected workshop. Paraplegics, unable to walk, who have to wear urinals, may solder at a bench, work a sewing machine with special attachments for its manipulation, paint luminous figures on watch-dials and enjoy to their benefit other similar occupations. Special arrangements can be made for their transport to and from work. With his fellows in protected employment, he can regain his self-respect by earning a competence and can contribute, too, to the social well-being of the disabled community.

**Acute Polyneuritis.**—This condition is probably identical with Landry's paralysis. Its cause, although undetermined, is almost certainly a virus infection. The fulminating case is beyond aid and kills the patient by paralysing the bulb. When the function of the medulla is threatened it may be necessary to place the patient in an "iron lung." For the usual case, however, this extreme measure is not required and, although paralysis has been rapidly progressive and profound at the height of the disease, the patient

can be assured that the process is a reversible one, but a long period of time will elapse before recovery. The general principles of treatment to be observed are those governing the case of the paralysed patient—attention to pressure points, passive movement of immobile limbs and alteration of position. Frequent alteration of posture in bed is the first line of defence against pulmonary hypostasis and infection. Vitamin B<sub>1</sub> has no specific effect in the treatment of this condition. If respiration has suffered embarrassment during the illness, great care has to be taken in convalescence because of the danger of respiratory infection. This applies with greater force when artificial aids to breathing have been necessary. Vitamin D affords some protection, but adequate rest should be prescribed and a process of “hardening” the patient should be ordered as in recovery from pulmonary tubercle.

### ANTERIOR POLIOMYELITIS

(See p. 41)

### TUBERCULOSIS INVOLVING THE NERVOUS SYSTEM

**Tuberculous Meningitis.**—Till recently the prognosis in tuberculous meningitis was invariably hopeless. The distressing symptoms of the disorder could be ameliorated to some extent by repeated lumbar puncture, which might have to be performed daily, and by strong sedation. Apart from careful nursing there was nothing further to be done, and death, which might occur in a few days or only after many weeks, came as a merciful release to the sufferer. The introduction of streptomycin has brought a faint hope that an antibiotic may soon be found which is specific against the tubercle bacillus. Streptomycin itself is probably not that antibiotic (see p. 130), but it is the most potent chemotherapeutic anti-tuberculous agent which has yet been discovered. A few cases of tuberculous meningitis have undoubtedly been cured by its use, though only after damage to the central nervous system has been so extensive as to make the cure of the acute infection a doubtful blessing. Extensive trials of streptomycin in tuberculous meningitis are at present being undertaken in this country under carefully controlled conditions, but at the time of writing the results are not available.

**Tuberculoma.**—When a focal tuberculous process occurs within the brain substance, the condition must be treated as a potential tumour of the brain. Decompression has to be undertaken if a tumour syndrome is apparent. Chronic tuberculomata may be excised, but not without impunity because of the danger of tuberculous meningitis. After neuro-surgery has restored normal circulation of the cerebrospinal fluid, the regimen is that for the treatment of tuberculosis (see p. 110). After the tuberculous process has become quiescent and is no threat to life, the focal symptoms of the lesion may require treatment. These symptoms include pareses and ataxias and, more frequently, epilepsy. The general rules which apply to the treatment of epilepsy are not modified by this particular cause of seizures.

**Pott's Disease.**—Involvement of the spinal cord in tuberculous caries of the spine is a late manifestation of the disease. Spinal compression can be prevented in the great majority of cases by early diagnosis and treatment

of the mischief in the spine. The general rules of treating paraplegia apply here (*q.v.*).

## TUMOURS OF THE NERVOUS SYSTEM

### CEREBRAL TUMOURS

The treatment of brain tumours depends upon the type and site of the tumour. There is no point in submitting a metastatic tumour of the brain to neuro-surgical intervention. If careful search reveals definite evidence of a primary growth elsewhere in the body, treatment is palliative and even decompression of the brain is not indicated. A short history and extensive focal signs of tumour offer little prospect for surgical relief. This prospect is diminished if mental confusion and general emaciation accompany the rapid development of neurological signs. Such cases should not be submitted to operation. Dysphasia and weakness of the limbs innervated by the dominant cerebral hemisphere are ill omens. Deep tumours involving the thalamic region and tumours infiltrating the brain stem defy surgical cure.

Once it has been decided that a tumour is worth the full neuro-surgical investigation, the onus of care lies with the neuro-surgeon. He may proceed forthwith to removal of the growth or may have to depend on ventriculography to delimit and localize the tumour. A certain number of tumours investigated by ventriculography are rejected for further operation. X-ray therapy may still be possible. Irradiation undoubtedly has its place in the treatment of cerebral neoplasms. Some tumours are too vascular to attempt removal. Rapid deterioration in the patient's condition during operation may frustrate the surgeon, as may sacrifice of valuable cerebral function. Glioblastoma multiforme will shrink with radiation, but relief from symptoms is so short-lived that it is inexpedient to irradiate this type of growth. Certain meningiomas respond well to deep X-ray therapy, and this form of treatment should be applied when surgical removal will wreck the intellect or cause profound paralysis. The results from irradiation of ependymal, pineal and oligodendroglial tumours are varied; although opinion is divided, X-ray therapy is frequently the only therapeutic weapon worthy of trial. Before therapy can be tackled, localization may have to be proved by ventriculography and decompression of the brain carried out. Reactive œdema to X-ray therapy is a commonplace in the treatment of tumours in other sites of the body and presumably brain tumours do not differ in this respect from tumours elsewhere. With heightened, increased intracranial tension, a further rise initiated by irradiation may have disastrous results unless room for expansion has been assured. The methods of decompression are a neuro-surgical problem.

If anything surgical has to be done to a brain tumour, it should be done quickly. Papilloedema is a sign of grave urgency. Delay in submitting the case to neuro-surgical attention prejudices sight, muscular power and co-ordination and even life itself. While attempting to be as constructive as possible, one must at the same time condemn certain practices prejudicial to the patient. It is far too common, to find that a patient with papilloedema as part of a cerebral tumour syndrome has had a lumbar puncture, in spite of full clinical awareness on the part of the physician. At times, this pro-

cedure kills the patient. If no papilloedema has developed in a tumour case, lumbar puncture is comparatively safe. The indications of increased intracranial tension, due to tumour, are usually so pronounced that the assessment of pressure by lumbar puncture is quite unnecessary. Rapid deterioration into coma, a few hours after lumbar puncture has been carried out, is quite a frequent catastrophe. With relief of pressure in the subarachnoid space, the tumour expands, becomes oedematous, and displaces the base of the brain downwards so that either a medullary or tentorial cone develops. Only the promptest action by the neuro-surgeon tapping a ventricle can avert disaster. The process of coning may occur spontaneously. Pending the arrival of the neuro-surgeon for this first-class emergency, 50 c.c. of 50 per cent. hypertonic glucose should be injected intravenously. The reduction in cerebral volume may tide the patient over the emergency until the surgeon taps the ventricle.

Successful removal of the tumour may enable the patient to return to his work, and indeed, to work more efficiently than for months before having had to cease his employment. Residual dysphasia of moderate degree will respond to the care of the speech therapist. Hemiplegia or paraplegia may indicate the need for vocational training or special employment. If epilepsy is a symptom of tumour, removal may not abolish seizures. Usually the epilepsy can be controlled by adequate anticonvulsant treatment. The patient should have a maintenance dose of phenobarbitone over the whole period of convalescence, and for two years, at least, after recovery.

### SPINAL TUMOURS

These tumours admit of successful removal only when they are extramedullary in origin. Surgical attacks on most intramedullary tumours are prompted more by daring than by logic; it is usually possible to tell by clinical signs and myelography whether the tumour is intramedullary or extramedullary. The intramedullary tumour may be treated by X-ray therapy, but results are scarcely satisfactory. Syringomyelia is such an intramedullary tumour; after clinical delimitation of the extent of the lesion, X-ray is worth trying because it seems to slow down the process. The therapy can be repeated yearly as long as the skin stands up to the irradiation. Extramedullary simple tumours are among the most favourable in neuro-surgery, and, if taken early, can be excised with complete success. Some meningiomata within the spinal canal tend to recur after the surgical extirpation, but it is important to note that a proportion is radio-sensitive.

For the treatment of paraplegia, with bladder and bowel difficulty, the same principles as are described on page 865 should be observed. Special mention must be made of the dissociated type of anaesthesia which occurs in intramedullary tumours and is notable in syringomyelia. In the latter condition the lesion usually affects the cervical region of the cord. Pain and thermal sensibilities are lost over cervical and upper dorsal segments. Certain restrictions are imposed on the individual, who should not be allowed to use his hands for any occupation in which burning or injury is likely. The maintenance of sensations of posture and touch is consistent with finely co-ordinate and skilled use of the fingers.

## TRAUMATIC DISEASE

### THE POST-CONCUSSIONAL STATE

Few syndromes are more trying to treat than this. Effort expended is often ill rewarded because the condition is responsible for much invalidism and lost working time. The dilemma of organic and psychological alternatives as a basis for the interpretation of symptoms makes any therapeutic approach uncertain. On the psychological side, fear of insecurity and of physical and mental disablement perpetuates symptoms. Introspection can be lessened by  $\frac{1}{2}$  gr. (0.03 gm.) of phenobarbitone, thrice daily; but as soon as the drug is stopped, the picture is no better. Treatment is hindered by the all-too-frequent litigation with which these cases are associated. With compensation law in its present state, the sense of insecurity is fostered and the idea of persecution encouraged. Little help can be given until the award is final. When the problem of compensation complicates the issue, the doctor's duty is to press lawyers and patient for settlement. The patient must be made to believe that no progressive damage is occurring to his nervous system, and that activity, free from anxiety, cannot possibly harm him.

### CEREBRAL TRAUMA

Head injury with permanent brain damage is quite another matter. Closed and open head injuries alike may cause permanent damage. It is a curious observation that the more profound the traumatic defect, the less the tendency towards the picture of post-concussional syndrome. Among the symptoms which have to be faced are loss of memory, intellectual impairment and paralysis. The only method of treatment is to help the patient to adjust himself to his disability and, if possible, to see that he is suitably employed. The not-infrequent epileptic state of traumatic origin requires the exhibition of anticonvulsant drugs. Trauma may cause damage to basal ganglia with the development of an extra-pyramidal syndrome. Its treatment is the same as that for the rigidity and tremor of paralysis agitans and post-encephalitic Parkinsonism (see p. 862).

### SUB-DURAL HÆMATOMA

Many die because this condition is either unrecognized, or diagnosed too late; adequate treatment, of course, does not exist apart from the realization of the clinical possibility. Too often the condition is confused with intracerebral hæmorrhage or a rapidly deteriorating case of brain tumour. Surgical drainage of the hæmatoma offers the only relief. The results of such treatment are dramatic, because the patient in profound coma may recover consciousness on the operating table when the hæmatoma is being evacuated.

### TRAUMATIC CONDITIONS OF THE SPINAL CORD

So-called concussion of the spinal cord requires no treatment further than that which is applicable to the early stages of an acute myelitis. Fracture dislocation of vertebrae with compression of the spinal cord may have to be corrected operatively and fixed post-operatively by orthopædic means. There is little point, however, in tackling these surgical problems when

cord damage has been present for more than one or two days. The medical treatment of such conditions is that of paraplegia (see p. 864).

**Hæmatomyelia.**—Hæmatomyelia occurs as the result of trauma or increase in venous pressure, but pre-existing disease at the site of the hæmorrhage is usually presupposed. It is very doubtful whether exposure of the cord and evacuation of the hæmorrhage is of any value. The treatment resembles that of syringomyelia (see p. 868), with the exception that X-ray therapy has no effect.

## VASCULAR DISEASES OF THE BRAIN

### CONGENITAL ANEURYSMS

Treatment depends upon the severity of the symptoms. The aneurysm oozing a little blood into the subarachnoid space calls for the same measures as in convalescence from a more massive rupture. Coma from massive hæmorrhage may be the precursor of death unless intracranial pressure is relieved. Repeated lumbar puncture is recommended in a lowering of the level of consciousness and in the severe distress of meningeal irritation. The writer has once observed death from massive subarachnoid hæmorrhage within a few seconds after lumbar puncture. The alarm of this experience has made him more conservative but has not prevented him from performing the same manœuvre when the above indications were present.

The general management of a case of acute subarachnoid hæmorrhage is that of meningitis; rest in bed is essential after signs of meningeal irritation have disappeared. By this means the inherent danger of a sudden rise in blood pressure is minimized and spontaneous healing of the rupture is encouraged. For many months after an attack, excitement, temper and other exertions are potential dangers to the individual, who must be protected accordingly. Too much prohibition is to be avoided because it may cause an increase in emotional tension with all the visceral consequences of that state, equally prejudicial to natural healing.

There is much to discourage one from a fatalistic view of prognosis in congenital aneurysm. Apart from the fact that many symptomless aneurysms are discovered incidentally at autopsy and the knowledge that rupture may occur but once in the middle of a long life, the skill of the neuro-surgeon has given fresh hope and his opinion should always be obtained in the case of a young person who has had a recurrence of subarachnoid hæmorrhage.

The demonstration of the actual site of the aneurysm by arteriography may invite direct surgical attack on the lesion, or may indicate the expedient of ligating the carotid.

**Complications of Intracranial Aneurysm.**—Intracranial aneurysm may cause permanent diplopia. Even surgical attack on the aneurysm will not remove the ophthalmoplegia. The only solution to the problem of diplopia is to place a shield or frosted lens in front of the affected eye. The treatment of other complications of aneurysm, hemiplegia and dysphasia, does not differ from the treatment of these states due to other causes.

**Anterio-venous Aneurysm.**—When free communication exists between the internal carotid artery and the cavernous sinus, pulsating exophthalmos on the side of the lesion is evident. The condition should be tackled surgically

as soon as is practicable after the injury—the usual precipitating cause. Ligation of the carotid artery on the side of the lesion is the usual treatment. The operation is carried out after the patient has been conditioned to occlusion of the circulation by compressing the artery, for increasing periods of time.

### CEREBRAL HÆMORRHAGE, THROMBOSIS AND EMBOLISM

The prevention of vascular accidents within the brain has its place in practice. Restrictions on the routine of life are imposed in good faith. The patient is asked to lead the simple, quiet life, not to over-exert himself, nor engage in anxious or exciting activity. Further, certain food-stuffs are cut out of the diet. The multiplication of such prohibitions may be so wearing to the patient as to make a fatal cerebral hæmorrhage preferable to the miserable existence of trying to prevent catastrophe. The psychological effect of too much restriction is much worse for the patient than a *laissez-faire* attitude. It must not be concluded, however, that there is no sense in some of the rules formulated from time to time for the treatment of cerebral vascular disease. Moderation of activity is a necessary injunction; dietary restrictions should be only with regard to quantity and not to quality of food; over-indulgence in tobacco and alcohol is to be condemned.

On no account should a patient who is threatened with a cerebral vascular accident be told what his blood pressure is; once told, he expects to have a figure given at each examination. The resource of a physician is poor if he cannot control a patient without having recourse to data expressed in millimetres of mercury. The fear of cerebral vascular accidents is not an inconsiderable cause of their occurrence. Usually that fear is well founded when there is a strong family history of cerebral hæmorrhage. The psychological handling of such a case is far more important, and far more effective than the exhibition of drugs and the imposition of restrictions.

**Cerebral Hæmorrhage.**—No considerable hæmorrhage can occur, rapidly, within the substance of the brain without suspension of consciousness due to the embarrassment of the circulation at basal levels. The object of treatment is to prevent further rise in intracranial pressure from continuing hæmorrhage and, therefore, it is argued that one should reduce blood pressure. The writer is in doubt about this expedient. It is known that consciousness depends upon the integrity of mid-brain structures. The function of these structures is already prejudiced by the embarrassed circulation. If the blood pressure is lowered sufficiently, the circulation must be further prejudiced. A capsular lesion in itself is not mortal, but death occurs secondarily from interference with blood supply at hypothalamic levels. The value of venesection has never rested upon scientific demonstration and there is more to be said for a policy of leaving blood pressure well alone than there is for reducing it.

It is more logical to employ hypertonic therapy in cases of cerebral hæmorrhage. Such a procedure diminishes the œdema surrounding the vascular lesion. Rapid dehydration of the brain can be achieved by the intravenous injection of 50 c.c. of 50 per cent. glucose. Ampoules of 50 per cent. glucose are readily available and are useful in cases of cerebral emergency either from hæmorrhage or tumour. It should be recognized that the effects produced are but temporary, and after the fluid balance has



been restored, more severe œdema may follow. Not so drastic, but of great value, is the use of a retention enema of 50 per cent. magnesium sulphate. The value of lumbar puncture in cases of cerebral hæmorrhage is doubtful therapeutically for the same reason as in cerebral tumour. The contents of the brain may shift to give all the evidences of coning. If lumbar puncture is performed for diagnostic purposes, a fine-bore needle should be used and little fluid withdrawn. Treatment does not cease when the patient recovers consciousness. Rest is essential. Anything which will increase blood pressure is avoided. Functions of the bladder and bowels are watched and treated with care. Excitement is allayed by hypnotics and pain is relieved by codeine, alone or in combination with aspirin and phenacetin. Morphine should not be given as this drug tends to congest the cerebral vessels.

**Cerebral Thrombosis.**—Little can be done to arrest or diminish actual damage wrought in the initial stages of cerebral thrombosis. The usual injunction is to increase the blood supply to the brain and various vasodilators have been recommended. If vasodilator drugs do any good it is logical to suppose that carbon dioxide would work like a charm because it is the most powerful of all the vasodilators of the cerebral vasculature. Yet, to the writer's knowledge, no one has ever attempted to treat cerebral thrombosis by this means. Increasing the systemic blood pressure in the hope of improving the cerebral circulation has little justification because the damage has been done before any means of increasing circulation can be exhibited. It is extremely doubtful if any measure can overcome the local vascular conditions productive of thrombosis. Consideration should be given to reduction of surrounding œdema. The methods for reduction of that œdema need not be as vigorous as that described above in the treatment of cerebral hæmorrhage. Purgation meets the case and can be achieved by the use of magnesium sulphate by the mouth if the patient is conscious, or a hypertonic enema of the same substance if the patient is unconscious. (See Cerebral Hæmorrhage.) Heparin does not seem to have a place in the treatment of cerebral vascular disease.

The after-care depends largely on the nature of the residual symptoms. Activity need not be so restricted as in the case of cerebral hæmorrhage, but it is usual to protect the patient against undue stress and strain.

**Cerebral Embolism.**—Cerebral embolism should, from the neurological point of view, be treated in the same way as cerebral thrombosis. Attention will, of course, have to be given to the origin of the embolus and its pathological cause.

**Cerebral Arteriosclerosis.**—Although cerebral hæmorrhage and thrombosis are evidences of diseased blood vessels, profound degeneration of the cerebral vasculature can exist without the occurrence of major cerebral catastrophes. Dementia and confusion may demand institutional care, but often the patient with mild senile changes can be catered for at home.

#### LATE EFFECTS OF CEREBRAL VASCULAR CATASTROPHES

More severe results of gross damage to the brain from vascular lesions such as mental confusion, restlessness and incontinence, cannot be dealt with in the average home. The patient requires constant supervision, and

sedation must be readily available when necessary. Institutional care is the only real solution to such problems.

**Hemiplegia.**—From the first occurrence of hemiplegia, paralysed limbs should be moved passively through their whole range of movement. With the return of voluntary power, exercises should be prescribed. Loss of postural sensibility imposes on the patient a further load which may be removed by training the limbs to obey the eye. The amount which can be done for the hemiplegic depends more on his residual intelligence than on the efforts of his doctor.

**Asphasia and Dysphasia.**—The principles of treatment are described briefly later (see p. 886). Cases must be carefully filtered for the speech therapist. Results are obtained only when there is sufficient foundation to carry the superstructure of training. Furthermore, the gravity of prognosis must necessarily modify the expedient of submitting cases to speech therapy. There is no point in asking a therapist to undertake the task of building up speech in a patient who is likely to have a further cerebral accident within a short period of time.

## DEMYELINATING AND DEGENERATIVE DISEASES

### DISSEMINATED SCLEROSIS

It is difficult to assess the value of any form of treatment in this disease because of the tendency for spontaneous remission to occur. Much claimed for treatment in the past can be accounted for by the natural course of the condition. No general rules can be given. The symptomatology is so varied that treatment must be of a symptomatic kind. Among the drugs which have been tried are arsenic and quinine. The former can be taken by the mouth in the form of the liquor. Doses of 10 minims (0.6 c.c.), thrice daily, may be given for the first week of every calendar month. The vitamin preparations, particularly the "B" group, have had their vogue but do little more than to increase the feeling of well-being and possibly the appetite. Some rules have to be observed in the general management of the condition. Exertion should stop short of undue fatigue, but by no means should the patient be over-restricted in his activity. There is no evidence that strict rest does any good. Indeed, any length of time in bed makes the symptoms worse. There is good reason, during the acute phases of the disease, to confine the patient to bed for most of the time, but movements of which he is capable should be practised even during the worst periods. Frequently patients suffering from the condition have been told the diagnosis. Their reading and conversation have often put the gloomiest construction on the significance of symptoms. To such people, much reassurance is needed and this reassurance should be backed by the knowledge that there is a wide variation in the natural course of individual cases. Remissions can last for ten or twenty years and such a state as retrobulbar neuritis may be the only evidence of the disease in a whole lifetime.

So far as individual symptoms are concerned, nothing is known to influence the course of retrobulbar neuritis. Diplopia is treated simply by covering up the unsound eye. Spasticity and ataxia are helped by exercises and are aggravated by cold conditions. Incontinence requires the same general management as that in any paraplegia from other causes.

Many people with a history of disseminated sclerosis are able to carry on their normal occupations, and employment must be dictated by capacity for work.

### **NEURO-MYELITIS OPTICA. (DEVIC'S DISEASE)**

Treatment is confined to the care of the paraplegic symptoms and complications. There is no specific remedy.

### **PARALYSIS AGITANS**

The same principles apply as in the treatment of extrapyramidal syndromes following encephalitis (p. 862). Because of the fact that arteriosclerotic disease is often a contributory if not a causative factor, the general principles in treatment of the basic disorder should be observed (see p. 871).

### **PROGRESSIVE MUSCULAR ATROPHY AND AMYOTROPHIC LATERAL SCLEROSIS**

Nothing is known to influence the downward course of this condition. The exhibition of amino acids is based upon false evidence and is a waste of money. Vitamin "E" is in no better a position. Local stimulation and massage are contraindicated. The patient should be encouraged to indulge in moderate activity for as long as he is able. Emaciation in the later stages brings with it the danger from pressure sores which must be prevented.

In bulbar cases there is difficulty in swallowing. Tube feeding may be carried out in order to maintain nutrition. When this stage is reached the condition is so depressing and the outlook so hopeless that it does not seem worth while prolonging the patient's misery.

Scottish Council for the care of spastics has been formed with a view to the treatment of spastic cases and cerebral palsies generally.

**Other Cerebral Palsies.**—More often than not the spastic case is complicated by extrapyramidal or cerebellar disorders and, frequently, congenital athetosis can exist without any evidence of pyramidal tract involvement. These cases should be treated in the same way as spastics, always remembering that the mental defect imposes restriction on the selection of cases for educational treatment, which, as a general rule, is not worth while undertaking if the intelligence quotient is below 80.

## EPILEPSY

Epilepsy is not a disease but a symptom which many diseases have in common. The term idiopathic should therefore be replaced by cryptogenic as applied to epilepsy. Treatment must be directed at prevention or removal of the particular causes of epilepsy and reducing the liability to attack when radical help is impracticable.

### EPILEPSY OF UNKNOWN ETIOLOGY

**Prevention of Epilepsy.**—When epilepsy is a symptom of an hereditary disease such as tuberosc sclerosis, advice against procreation should be given. If the epilepsy is due to cerebral trauma, cerebral vascular change or inflammatory disease, there is no reason, other things being equal, to advise against having children. The most difficult decisions are in cases of unknown etiology. Frequent attacks difficult to control by anticonvulsant drugs, the incidence of epilepsy of unknown etiology in near relatives and the occurrence of mental deterioration in spite of treatment are all contraindications to marriage.

**Management.**—No epileptic should be allowed to drive a car, to swim, or to pursue the business of a slater. Such prohibitions are obvious and need not be enumerated. Very often the epileptic insists on activities which may involve himself and others in danger in order to vindicate himself and compensate for his affliction. Wrong as it is to allow such activity, it is grievous to restrict him any more than is necessary.

Life to the epileptic is a constant hazard at home, in the street, at work and at play. When fits are well under control little restriction is needed; he should be encouraged to lead as normal a life as possible. Frequent attacks intractable to treatment and mental deterioration demand institutional care. Many cases require protected employment; for others, occupational therapy, preferably of a remunerative kind, can be arranged at home. Management of the epileptic must always depend on an adequate conception of the disability. A protracted aura of constant occurrence extends liberty; sudden loss of consciousness imposes restrictions. Habitual nocturnal fits are consistent with a full daily round of activity but may demand attention lest the sufferer turn on his face and smother himself because he lies on a soft instead of a hard pillow.

Management of the major seizure consists in preventing the convulsion causing injury. Some form of gag—a padded spoon handle—is put between the teeth to prevent biting the tongue. Excessive movement of limbs and spine can be prevented by forcible fixation. The occasional over-opening

of the mouth should be controlled to avert dislocation of the jaw. These remarks apply particularly to the handling of therapeutic convulsions which are the most violent of epileptic attacks. When the convulsive stage has passed, the air passages must be kept free. Due appreciation of the relative seriousness of the various causes of respiratory embarrassment will ensure removal of a broken denture from the region of the fauces before loosening a tight collar; removal of mucus or regurgitated gastric contents from the throat must precede cutting corset laces. Each fit must be observed until the patient drops off into a natural sleep or until the state of automatism has passed. The patient may harm himself needlessly in such automatic episodes because of neglect. The rationale behind treatment of epilepsy must be to administer drugs which will raise the convulsive threshold and avoid any measure which will lower that threshold. The goal of treatment is to make the epileptic able for remunerative work. Hence fits must be reduced to a minimum severity and frequency if they cannot be abolished altogether. Each epileptic fit in itself lowers the convulsive threshold; each successive fit is encouraged by its predecessor. Drugs which raise the convulsive threshold are the barbiturate group, diphenylhydantoinate (phenytoin), and bromide.

The sheet anchor in treatment is the barbiturate group. Epileptics with infrequent and limited seizures may become symptomless on half a grain (0.03 gm.) of phenobarbitone per day. With increasing severity and frequency of seizures correspondingly larger doses of phenobarbitone are demanded. It is better to exceed the maintenance dose for some time than never to reach it at all. The dose of 8 gr. (0.5 gm.) per day is seldom exceeded and it is scarcely expedient to do so. There is no advantage in giving phenobarbitone sodium, the soluble form of the drug. Indeed, its therapeutic value is reckoned at 10 per cent. less than phenobarbitone itself. Phenobarbitone is very effective in combination with phenytoin. A moderate epileptic responding, let us say, to a grain (0.06 gm.) of phenobarbitone, thrice daily, without, however, having his seizures completely abolished, may be symptomless with 3 gr. (0.18 gm.) of phenytoin substituted for the midday dose. Only trial and error in cases difficult to control can establish the proper maintenance dose. Phenobarbitone itself is, in most cases, well tolerated by the epileptic. Some, however, become drowsy even with small doses. Phenytoin is more anticonvulsant and less hypnotic than phenobarbitone and, consequently, it is the drug of choice when phenobarbitone produces somnolence inconsistent with reasonable enjoyment of life. Phenytoin 3 gr. (0.18 gm.) in a capsule, thrice daily, is the recommended average dose when no other drug is being administered. It is possible to push the dose to 15 gr. (0.9 gm.) daily or to combine 9 gr. (0.5 gm.) with 3 to 4 gr. (0.18 to 0.24 gm.) of phenobarbitone daily.

Many practitioners do not realize the importance of maintaining therapy long after the occurrence of the last seizure. Two years are scarcely long enough in many cases. Never should the physician be deluded by a false sense of security when therapy has been successful in abolishing seizures for a few months. If, after having maintained treatment assiduously, he should withdraw anticonvulsant drugs suddenly, he will merit the anxiety of dealing with the not-infrequent status epilepticus which his indiscretion has induced.

Bromide has a time-honoured use in epilepsy. Seldom does it prove

more effective than phenobarbitone or phenytoin. It may be given with phenobarbitone as in the following prescription:

R	Sod. Brom.	.	.	.	.	gr. 10 (0.6 gm.)
	Phenobarb. Sod.	.	.	.	.	gr. 1 (0.06 gm.)
	Ext. Glycyrrh. Liq.	.	.	.	.	℥ 30 (1.7 c.c.)
	Aq.	.	.	.	to	fl. oz. $\frac{1}{2}$ (14.2 c.c.)

If bromide is used when other measures have failed, it is made more active therapeutically by the withdrawal of salt from the diet. Antagonist to the hypnotic effect, but not to the anticonvulsant properties of phenobarbitone, is amphetamine (Benzedrine). This drug has a beneficial activity, particularly in cases suffering from petit mal as well as grand mal. The dose of anticonvulsant drug may be varied routinely with advantage when there is a cyclical incidence of the seizures in women at the times of the menstrual periods. That variation may mean the addition of  $\frac{1}{2}$  to 1 gr. (0.03 to 0.06 gm.) of phenobarbitone daily for two or three days before or after the period. The menstrual function is associated with disturbances in water balance and in some instances it is sufficient to limit fluid intake at the time of the period without adding to the routine maintenance dose. Dehydration and fasting have had their vogue as means of combating epilepsy. The acidosis of fasting raises the convulsive threshold as does the ketogenic diet—a method of treatment largely given up because of its inconvenience, the discomfort caused to the sufferer and the superiority of other methods.

The epileptic and his relatives may not accept readily the necessity of prolonged treatment. Objections are raised to the constant taking of drugs as a matter of principle. These objections are sustained by arguments that drugs cause mental deterioration. The evidence is that phenobarbitone does not cause mental deterioration. Deterioration is much more likely without anticonvulsant treatment as each seizure prejudices cerebral function and may cause irreversible structural damage. Difficulties arise when toxic manifestations peculiar to the drug exhibited make their appearance. Bromide is the chief offender and raises alarms by producing a toxic psychosis with confusion and hallucinations. The bromide must then be stopped forthwith and abundant fluids and sodium chloride should be given to aid elimination. From the skin manifestations of bromide intoxication, the patient may be partially protected by 3 minims (0.2 c.c.) of liquor arsenicalis three times a day. The barbiturates are usually well tolerated and their administration is seldom attended by any ill effect. Phenytoin may cause swelling of the gums, which is no reason for suspending its administration when the drug is more effective than other measures. Sometimes, but rarely, ataxic symptoms such as diplopia, headache, gastrointestinal disorder may occur as toxic effects from phenytoin. Such symptoms necessitate withdrawal of the drug and substitution of adequate doses of barbiturate. Very occasionally the exhibition of phenytoin is attended by an increase in the number of seizures. Again the drug must be withdrawn and an effective amount of barbiturate substituted.

#### STATUS EPILEPTICUS

No half measures are entertained in dealing with this dangerous condition. Intravenous sodium phenobarbitone should be given whenever the

condition is established. The dose is 3 gr. (0.18 gm.), repeated if necessary, and the drug is available in appropriate ampoules for this particular purpose. Fast injection may cause unnecessary anxiety by depressing respiration and cardiac activity. Intravenous phenobarbitone may be sufficient to control the status, but oral administration must follow until the patient is stabilized on a maintenance dose. Most cases, however, should have paraldehyde as well as intravenous phenobarbitone. Six drachms (21.6 c.c.) of paraldehyde in 8 oz. of water should be given rectally, or 8 drachms (28.4 c.c.) in 8 oz. of water if no intravenous phenobarbitone has been given previously. Enemata of 2 to 4 drachms (7.2 to 14.4 c.c.) can be repeated at two- to four-hourly intervals depending on the response of the patient as judged by the severity and number of subsequent fits. Of real danger is the onset of hyperthermia in status epilepticus. The metabolic cost of seizure after seizure sends up the blood temperature to such a degree that the thermal regulatory functions of the hypothalamus are impaired. This impairment creates a vicious circle which must be broken by strenuous measures. Tepid sponging when the temperature reaches 101° F. may do much to prevent a further rise. When temperatures reach 106° or 107° before treatment can be applied, tepid sponging is useless. All clothes and coverings should be removed from the patient, his skin should be rubbed vigorously until red, and cold water applied to the body surface exposed to a stream of moving air from electric fans.

### EPILEPSY OF KNOWN ETIOLOGY

Cerebral trauma, meningeal infection, encephalitis, sub-dural hæmatoma, tumours simple and malignant, cysticercosis, vascular disease, neuro-syphilis, neuro-tubercle, uræmia and hypoglycæmia can cause epilepsy. The treatment becomes primarily, when feasible, the treatment of the causative condition. Tumours can be removed, infections can be attacked by chemotherapeutic and specific drugs and sub-dural hæmatomata can be drained. The treatment of cause is, however, scarcely enough. Surgical removal of a tumour may leave a scar as epileptogenic as the tumour itself. The surgical treatment of scars from cerebral injury, although sometimes followed by a measure of symptomatic relief, is still a matter of new scars for old.

Fits in rapidly improving neuro-syphilis undergoing specific treatment demand little treatment directed towards their abolition. The occurrence of fits in a case of meningitis amenable to chemotherapy does not imply a long and rigorous course of anticonvulsant therapy. Irreversible scar formations, whether caused by trauma, infection or degenerative vascular disease known to be epileptogenic, require the same assiduous treatment as the epilepsies of unknown etiology. Seizures in cases of cerebral tumour should be dealt with by anticonvulsant drugs before and after the tumour has been dealt with surgically. The same principle applies with even greater force to the epilepsies of cerebral abscess. Certain cases of meningioma and of angioma respond clinically to X-ray therapy; if epilepsy be part of the clinical picture, X-ray treatment almost invariably is accompanied by a regression of epileptic symptoms, but seldom allows a cessation of anti-convulsant treatment.

## PETIT MAL

Anticonvulsant drugs have little or no effect on petit mal, indeed often the symptom may be accentuated by their use. The exhibition of amphetamine was suggested because electroencephalography showed, in petit mal, rhythms resembling those of sleep. This drug has proved itself of value in cutting down the number of attacks—it should be prescribed in 5 mg. doses on awakening and at noon to start with and, later, the amount can be increased to 25 mg. daily if indicated. It is not advisable to give the drug after 4 or 5 p.m. because of its antihypnotic effect. Usually the drug is given in combination with a maintenance dose of phenobarbitone. Caffeine citrate in doses of 3 to 5 gr. (0.18 to 0.3 gm.) has some effect in reducing the number and severity of attacks.

Recently it has become apparent that a further advance in the treatment of epilepsy has been made. In the search for new analgesic drugs a substance 3, 5, 5, Trimethyloxazolidine 2, 4, dione (Tridione, Abbott), was found incidentally to be of real value in epilepsy. Often the effect of its exhibition is quite dramatic in arresting petit mal attacks and psychomotor equivalents when all other means have failed. Tridione should never be the first approach to the problem of therapy. Only when failure with other drugs is evident should Tridione be used. The dose is 0.3 gm. for a child, and, for an adult, 1 to 2 gm. per day. Of little value in grand mal, Tridione is prescribed along with phenobarbitone or phenytoin when grand and petit mal co-exist. For somnolence, amphetamine may be added.

Tridione is a toxic substance and some deaths have been reported as a result of its use. Agranulocytosis is a real danger arising out of the toxic effect of the drug on the bone marrow. General dermatitis may complicate the picture and the drug should be withdrawn at the first sign of a skin eruption. A side-effect—the “glare” phenomenon which is a hypersensitivity to light—does not necessitate withdrawal of the drug unless the symptom proves of great distress to the patient.

*Pyknolepsy* is a rare condition. If the criterion is satisfied that the sufferer is conscious during the attack, no treatment is necessary. If there is any doubt about the condition it should be regarded and treated as petit mal.

## MIGRAINE

The treatment of migraine consists of avoiding the precipitating causes of an attack, if precipitating causes are clearly known. Any error in refraction should be corrected; over-fatigue, physical and nervous, and indiscretions of diet should be avoided. Any disease of the accessory nasal sinuses should be dealt with. If there is a history of dyspepsia and flatulence the gall bladder function should be investigated and, if disordered, treated.

For the acute attack many find relief in taking a powder consisting of 10 gr. (0.6 gm.) each of phenacetin and aspirin with 5 gr. (0.3 gm.) of caffeine. The sufferer should always have this powder with him and should lie down whenever the attack comes on. More severe cases of migraine do not respond to a simple powder of this kind and the only relief possible may be from ergotamine tartarate by subcutaneous injection in a dose of  $\frac{1}{4}$  to  $\frac{1}{2}$  mg. The patient should be taught to give the injection himself.



The dose may be repeated within an hour. Milder cases respond to ergot-amine tartarate by mouth. When taken orally the dose is 2 mg., which can be repeated in one or two hours.

Recently urea has been recommended for the treatment of migraine. It is certainly worth a trial. Sixty gr. (3.9 gm.) of urea, thrice daily, may be given to the patient whose life is rendered miserable by frequent attacks. There is no harm in continuing the administration of urea over a long period of time.

### VERTIGO

Vertigo of labyrinthine origin is a disabling and alarming symptom and carries with it symptoms of psychological stress. When attacks are frequent the patient should be given as a routine, 15 gr. (0.9 gm.) of ammonium chloride in capsule, thrice daily, for periods of three days, alternating with periods of three days' rest from the drug. Salt should be excluded from the diet. This treatment is designed to reduce endolymphatic pressure.

It is noteworthy that many sufferers from migraine find their symptoms disappear about the age of forty, only to be replaced by labyrinthine vertigo.

In intractable cases the surgical procedure of sectioning the eighth nerve in the posterior fossa may be carried out, provided the disturbance can be traced to one internal ear, and provided the other ear is intact.

## DISORDERS OF MUSCLE AND THE MYONEURAL MECHANISM

### MUSCULAR DYSTROPHIES

For the muscular dystrophies there is no satisfactory specific treatment. From the idea that ingestion of amino-acids might spare muscle by providing readily available protein came the therapeutic trial of glycine. There is no evidence that such treatment can either reverse or arrest the dystrophic process. On the assumption that a vitamin deficiency might be present,  $\alpha$ -tocopherol (vitamin "E") has been tested and found wanting. Deformities and contractures should be prevented by exercise as long as the patient is able to execute the necessary movements, and by passive movement when the limbs become immobile. Myopathies may be so slowly degenerative that their care is a problem to those who have to look after them. Employment under protected conditions can be given to a few; the best form of treatment is to provide them with work within their limited capacity.

### DYSTROPHIA MYOTONICA

(*Myotonia Atrophica*)

No specific treatment can arrest or modify the course of this disease. Any influence exerted by drugs is purely symptomatic in effect. The increased muscle tone and slowness of movement can be reduced by giving 10 gr. (0.6 gm.) of quinine bihydrochloride once a day. Lenticular cataract, an early accompaniment to the muscular disorder, can be dealt with by the ophthalmic surgeon. There is no further abnormality in the refractive media or in the retinal structure.

### MYOTONIA CONGENITA

Myotonia congenita has a muscular disorder similar to that of myotonia atrophica; it is treated in the same way.

### MYASTHENIA GRAVIS

Myasthenia gravis responds in different degrees to treatment. The rationale of treatment is to neutralize the effect of cholinesterase by the administration of eserine or its more effective analogue prostigmin. In most cases, the subcutaneous injection of 2 mg. of prostigmin has the dramatic effect of improving the myasthenic condition, sometimes achieving complete normality within fifteen minutes. Prostigmin should be given with atropine,  $\frac{1}{150}$ th of a grain (0.4 mg.) of atropine sulphate, to prevent vagal effects—intestinal colic and cardiac inhibition with sweating. Administration of the atropine should precede that of prostigmin by half an hour. Prostigmin, fortunately, is active by the mouth and 15-mg. tablets are available. Eight to ten of these tablets can be given during the course of the day. Prostigmin is expensive and there is always the temptation on the part of the patient to cut down dosage. Every possible care should be taken to see that the maintenance dose of prostigmin is continued. It is quite clear that some cases of myasthenia gravis, in spite of some response to treatment, degenerate and ultimately atrophic changes occur in the affected muscles. These cases are extremely resistant and cannot be prevented by the most generous administration of prostigmin. Adjuvants to prostigmin are 20 gr. (1.2 gm.) of potassium citrate and  $\frac{1}{2}$  gr. (0.03 gm.) of ephedrine three times a day. In the resistant case, the use of these drugs in combination with prostigmin is justifiable. One modification of treatment may have to be followed when the muscles of deglutition are so weak in the morning as to render impossible the use of oral prostigmin. In these instances, the subcutaneous injection of prostigmin should start the day.

Because of the very high incidence of thymus tumour in myasthenia, the operation of thymectomy has been introduced even for cases in which no thymic tumour can be demonstrated. The procedure would be a formidable one for a normal person and is naturally more serious for a myasthenic. It should, therefore, only be contemplated when the general condition of the patient has been raised to the highest possible point by the use of prostigmin, ephedrine and potassium salts. Further, the operation should only be undertaken by a surgeon thoroughly conversant with the best modern technique for thymectomy. In experienced hands a greater or less degree of improvement may be anticipated in a considerable proportion of cases, and in a few this improvement is very dramatic. Some improvement has also been occasionally observed when X-radiation has been applied to the region of the thymus.

In the general conduct of life, the patient should observe economy of muscular effort.

### FAMILIAL PERIODIC PARALYSIS

This rare disease has no specific cure, but symptomatic relief is afforded by the administration of potassium chloride in 12-gm. doses. This salt can be given just before retiring, and in the morning, if the patient is paralysed,

on awakening. The action of the potassium is to increase neural and muscular irritability.

### NEURITIC SYNDROMES

Peripheral nerves may be damaged by mechanical causes, by infections and by toxins, endogenous and exogenous. They may degenerate as the result of specific nutritional deficiency or as the result of diminished blood supply. Beyond these there is a shrinking, ill-defined group of distressing, painful conditions, conveniently, perhaps ignorantly, dubbed as neuritis of rheumatic origin.

When muscle is paralysed as the result of a damaged innervation, posture must be adjusted by splinting if necessary, so that the affected muscle is taken off the stretch. Experimental work has shown that denervated muscle does not lose bulk as rapidly when effective daily electric stimulation is given and that end results are better, too, when time is allowed for regeneration. Therefore electrical stimulation should be carried out, as in certain neuritides, as soon as the pain of stimulation can be tolerated. The paralysed limb should be moved passively through as full a range of movement as possible. This need be done but once daily to prevent contractures and fixations secondary to immobilization. Lastly, with regard to muscle recovery, one flicker of voluntary movement is worth twenty electrical twitches. When muscle is recovering, exercises designed to bring affected muscles into play should be prescribed. Massaging paralysed muscle is without beneficial effect on the muscle and bears no scientific justification for its use. Fixation of a limb, however, carries with it secondary vascular effects. The skin becomes cold and discoloured and at times œdematous. These changes are lessened by effleurage; consequently the nutrition of the skin may be helped by that form of massage.

### TRIGEMINAL NEURALGIA

Paroxysmal trigeminal neuralgia, or tic douloureux, is characterised by such exquisite pain that release earns embarrassing gratitude. Milder cases respond to 10 minims (0.6 c.c.) of the tincture of gelsemium thrice daily. Frequently the pain, in spite of medicinal treatment, recurs or is uninfluenced. Injection of absolute alcohol may then be considered. Injection of the third division of the nerve should be entrusted to the experienced. The danger of the procedure in the hands of the novice is damage to cavernous sinus structures with consequent ophthalmoplegia. Too much alcohol given when the point of the needle has just penetrated the foramen ovale kills all the cells of the Gasserian ganglion, renders the cornea anæsthetic, and may produce neuro-paralytic keratitis. Injection of the second division is less frequently successful than injection of the third. When the trigger point is within the territory of the second division near the ala nasi, injection of the intra-orbital nerve with the needle in its foramen of exit often affords complete relief for many months. If pain is experienced in the distribution of the first division, complete destruction of the ganglion by alcohol is the only solution if injection is to be the method of treatment. This last operation in the hands of expert or tyro carries with it the danger of neuro-paralytic keratitis. Some protection against the development of this distressing condition is afforded by wearing spectacles with a shield on the

affected side. This shield is attached to the spectacles' rim and is made to fit closely to outer margin of the orbit. Even this precaution may not succeed. At the first sign of neuroparalytic keratitis, the eyelids should be stitched together. Neuroparalytic keratitis is never painful. Reddening of the conjunctiva and corneal ulceration in the anæsthetic eye are the precursors of ophthalmitis and loss of the eye.

To describe the technique of these injections is beyond the scope of this work. It is well to know that they have their place in treatment. By far the most satisfactory method of treatment is differential section of the sensory root of the nerve by open operation. This operation may be at times one of emergency as there is no more urgent symptom for which so much can be done than the pain of trigeminal neuralgia. If a doctor submits a case of facial pain other than that of trigeminal neuralgia or malignant disease of the jaws or tongue to injection with alcohol or operation, he will deserve the fate of having to listen to the interminable complaints of his victim.

#### HERPES OF THE FIFTH CRANIAL NERVE

This distressing condition may give rise to much disfigurement and pain. During the acute phase the skin should be kept dry and dusted with a simple dusting powder. Pituitrin, 1 c.c. subcutaneously, is recommended as a means of alleviating pain in the acute phase. When this fails, phenacetin in 25 gr. (1.5 gm.) doses is usually effective, but may have to be supplemented by codeine or even morphine. Post-herpetic neuralgia is a baffling sequel. The actual pain is so disagreeable that the sufferer develops a neurosis more difficult to treat than the pain. Application of percaïne ointment,  $\frac{1}{2}$  per cent., gives some relief by cutting down the cutaneous stimulation which facilitates spontaneous pain. Operations on and injections into the Gasserian ganglion or its roots are ill-advised; the condition usually subsides even after a year from the acute attack. The most intractable post-herpetic neuralgia usually occurs in the first division of the trigeminal. In virtue of the site of pain the sufferer conceives some serious mischief within the skull itself; he believes the magnitude of the disturbance must equal that of the symptom. Assurance must go hand in hand with any physical or medicinal treatment. Radiation of the Gasserian ganglion claims some success, but its value is doubtful because of the general tendency to spontaneous improvement. Ulceration of the cornea is another unfortunate sequel of the acute attack of herpes of the first division of the fifth cranial nerve. The problem concerns the ophthalmologist, who should always be consulted when the cornea is damaged.

#### BELL'S PARALYSIS

The majority of cases recover spontaneously without any special attention to treatment. To decompress the facial nerve by opening the facial canal within a day or two of the onset is bold in the extreme. Counter-irritation applied over the region of the stylo-mastoid foramen has little to commend it. Treatment should be dictated by the clinical state. For the milder case with little loss of muscle tone and with beginnings of recovery, exercises in front of a mirror are sufficient. Lax and grossly paralytic facial muscles require splinting and electrical stimulation. The

actual splint takes the form of a rubber-covered wire bent to form a "U" at one end and a spectacle leg at the other. The "U" bend hooks into the paralytic angle of the mouth and the spectacle leg fits over the ear to exert traction on the angle of the mouth and restore facial symmetry. Electrical stimulation should be continued until within some weeks the patient is able to undertake voluntary movement before a mirror. There is no danger in overdoing electrical stimulation. The idea that the so-called post-paralytic contracture of the face is due to electrical treatment is self-reproachful fantasy. The contracture occurs because of random regeneration of the facial fibres after a pathological process has destroyed the fascicular pattern of the nerve. Nothing can be done to correct the results of random regeneration. Should no regeneration occur, medical treatment is of no avail and the patient should be referred to a plastic surgeon for the insertion of a fascial sling. Insertion of a nerve graft into the facial canal cannot achieve anything better than random regeneration and total failures are many. In all cases of facial paralysis of the lower motor neurone type accompanied by defective corneal sensation, the eyelids on the affected side should be stitched together.

### **COSTO-CLAVICULAR SYNDROMES**

Congenital abnormalities in the region of the neck and the thoracic outlet may be symptomless for years. When the tone of the muscles of the shoulder girdle is lowered from whatever cause, symptoms referable to the arms make their appearance in the presence of previously symptomless congenital abnormalities. Treatment of these syndromes is primarily medical. If the syndrome is developed through excessive work, *e.g.* lifting heavy loads, that cause must be removed, therefore rest is the first essential. Rest will permit the distorted neural structures to recover; with recovery, symptoms disappear.

If the patient has lost his muscle tone through debilitating illness, convalescence from that illness has not been long enough and further rest must be prescribed. After alleviation of pain and paræsthesiæ by means of rest, exercises calculated to restore muscle tone to the shoulder girdle should be given. Under no circumstances should surgical intervention take precedence over these simple measures. Indeed, such operations as removal of cervical ribs and cutting of scalene bands fall short of ideal therapy. These operations, although they may remove symptoms, cannot pretend to deal with the precipitating cause of the complaint.

### **MUSCULO-SPIRAL PARALYSIS**

*(Saturday-night Palsy)*

This is best treated by resting the extensors of the wrist and fingers in a cock-up splint. If the paralysis is profound, electrical stimulation of the affected muscles should be carried out assiduously. Whenever voluntary power begins to return, remedial exercises should be instituted.

### **TRAUMATIC ULNAR NEURITIS**

In subjects with a wide carrying angle and hyperextensible elbows, the ulnar nerve is mobile and easily dislocated from its bed in the epicondylar

groove. Because of this anomaly the ulnar nerve is liable to injury from pressure at the elbow. In some occupations pressure on the ulnar nerve at the elbow can scarcely be avoided. Treatment is directed to removing the cause by instructing the patient about those postures which render the ulnar nerve liable to pressure. If these causes can be removed, further treatment may be unnecessary. When the ulnar nerve is thickened and mobile at the level of the elbow, prevention of trauma in everyday life may be impossible. Under such circumstances satisfactory results follow transposition of the ulnar nerve from the epicondylar groove to the anterior aspect of the forearm. Burying the nerve in the head of the flexor-pronator group of muscles is an additional protection. Weakness and atrophy of the intrinsic muscles of the hand should be treated by exercises and appropriate occupational diversion.

### MEDIAN NERVE PALSY

Recently a syndrome of the median nerve has been described. The symptoms are produced by pressure on the nerve as it travels under cover of the anterior carpal ligament. The recommended procedure of cutting down on the nerve at the site of the lesion and freeing it in its bed should be tried only after rest has failed. It is but reasonable to assume that prevention of relative movement between the nerve and the tissues surrounding it will permit œdema and vascular engorgement to subside. The first treatment, therefore, should be to fix the wrist by splinting. From personal experience, this method of treatment is effective without having recourse to operative interference. When pain and paræsthesiæ have disappeared after rest, passive movement and exercises are instituted.

### TRAUMATIC, MEDIAN AND ULNAR LESIONS WITHIN THE HAND

Traumatic, ulnar and median lesions in the hand may occur from occupational causes such as wielding a pick-axe or operating automatic riveting machines. Cessation of work is the first essential in treatment. Rest to the affected part, by splinting if necessary, should follow. Complete restoration of function after rest can usually be ensured by remedial exercises and electrical stimulation.

### HERNIATED NUCLEUS PULPOSUS

Among the causes of sciatica, retropulsion of an intervertebral disc must take first place. The condition has been known and recognized for long enough to free it from the suspicion with which orthodoxy scorns a new cause for an old symptom. The high frequency of herniated discs in lumbago and sciatica does not alter the fact that most cases of lumbago and sciatica were cured spontaneously before herniations were first described. This simple truth should be the rational basis for treatment. Apart from exploration and removal of the offending protrusion, is there any way to cut short the symptom of sciatica? Formerly some credit was given to the removal of septic foci as an efficient means of curing sciatica. It now seems quite clear that the rest in bed necessitated by the removal of septic tonsils or other foci was the effective measure. Many cases in self-defence sought the refuge of bed to escape from the assaults of manipulators and nerve-stretchers

and to find alleviation of suffering in rest. Once the diagnosis has been established, rest in bed should be ordered. Fracture boards are placed under a hair mattress and only one pillow is allowed. The patient may be permitted to roll on to either side. He is not permitted to sit up; his spine must be kept as nearly horizontal as possible. Bed-pans and urinals are part of the routine. After, or during, the third week of this treatment, exercises in bed are ordered; these are graduated and the patient is allowed up at the end of the third, or during the fourth week. The whole object of treatment is to prevent relative movement between the herniated disc and the affected nerve root. The affected root is oedematous, and oedema and pain are perpetuated as long as relative movement occurs. With rest, the oedema disappears and the root adapts itself to the deformity. After the period of rest has been completed the carrying or lifting of weights with the spine flexed is forbidden for some further three to six weeks. The importance of prevention of flexion must be emphasized because this movement precipitates the condition. Indeed, some recommend rest in hyperextension by having the patient lie with a pillow under the lumbar region.

The initial exquisite pain of lumbago and sciatica is sufficient to immobilize the patient. Any movement causes pain and reflex spasm at the site of damage. Morphine should not be given, even although the pain may appear to demand it. Aspirin, phenacetin and codeine sufficiently often and in adequate amount are usually enough to cope with the pain. Twenty gr. (1.2 gm.) of phenacetin at a single dose can be given and may be repeated when the pain recurs.

The small percentage of cases not responding to the treatment indicated above is dealt with surgically, as are those few in whom paralysis is marked. When paralysis is extensive, the earlier operation is tackled the better.

Sciatica is a symptom often associated with psychological overlay. Not merely does the sufferer have to contend with recurring excruciating pain, but he has to face up to the fear which his symptom engenders. The layman must explain his pain to himself. This he does in terms of something happening to his spine. Anything which aggravates his pain is a source of terror to him. That terror has its physical counterpart in increased muscular tension and sometimes actual tremor. The patient shuns all movement of the spine, fearing to cause permanent damage to his spine or to his nerves. He may hesitate to cross a street because of the possible necessity for quick movement; so fears multiply until he is a nervous wreck. These cases must be taken in hand. Assurances must be given of the stability of the spine and of the forces which protect it against damage. Much residual pain is caused by local boarding of muscle through fear; that fear must be allayed. A little thought and time devoted to symptoms at the psychological level will enable the physician to banish many a phobia when these are causally related to the patient's conception of the malady.

## SPEECH THERAPY

About 1 per cent. of school children stutter and a further 3 to 5 per cent. have other defects in speech. Subjected to merciless mimicry from school-mates and unfeeling relatives, the sufferer becomes a creature of retarded progress and warped personality. Adults may be victims of speech defect continued from youth or acquired in maturity. Their lot is no less difficult;

they are hampered in all self-expression by word of mouth. Not merely the number afflicted but the magnitude of the individual problem make the need for speech treatment clamant.

Too often in the past the sufferer has been exploited by quackery at the hands of the unqualified. To-day the speech therapist is an officially recognized medical auxiliary; her special training in normal and disordered speech, relevant anatomy and physiology, psychology and educational method fit her to tackle the problem.

Speech clinics have now been established at the main teaching hospitals and the treatment of children is part of the school health service.

The selection of material for the speech therapist depends on the cause of the defect and the outlook for the individual. One must exclude such cases as dysarthria from bulbar paralysis and dysphasia from progressive disease of the brain. Cases of cleft palate, stuttering or impediment from cramping of the muscles of articulation, dysphasia following head injury or with static lesions of the brain are all candidates for treatment. The potential case should be presented to the therapist as complementary to medical or surgical alleviation of the causative condition. An adequate account of the condition from the practitioner's angle should accompany the patient. This obligation is reciprocated by the therapist who in return will seek guidance of the doctor in the management of the case.

The methods used by the therapist vary with the cause of defect. In deformity of the upper respiratory tract, treatment is directed towards producing the best articulate sound consistent with the deformity, by exercises in the use of a limited speech equipment.

The spasms and tics of stuttering demand exercises in progressive relaxation of the whole voluntary musculature. These exercises combat spasm in the muscles of articulation and rid the patient of that general muscular tension which is the result of emotional strain. In complete muscular relaxation, for some unknown reason, the storms of psychological conflict abate and the mind responds more readily to suggestion and instruction. Because the dysphasic patient is rendered worse by emotional stress, relaxation therapy becomes an important means of helping him.

Intellectual speech difficulties caused by lesions of the dominant hemisphere make greater demands on the skill and experience of the therapist. She has to use educational technique to facilitate activity over the associative pathways remaining intact. The patient is made to associate various sensory experiences of one object with one another and with the appropriate word symbol. Patients with inferior cerebral equipment have to go back to learning a language afresh.

## WRITER'S CRAMP

Gowers gave a classical description of this condition and showed how bad posture and stilted movement were the factors responsible for its origin. Gloomy as the outlook is, treatment has been no more than toying with the situation. Stop writing altogether; learn to write with the left hand; give soothing baths to the hand and forearm; change your occupation; these are some of the ineffectual shifts recommended.

In the past insufficient emphasis has been laid on the fact that stuttering and writer's cramp belong to the same group of disabilities. Writing and



speaking are motor forms of expression in language. Writer's cramp and stuttering are muscular spasms which interrupt the normal flow of writing and speaking and may postpone or prevent the initiation of these acts. Exactly the same kind of treatment is required in both, clearing the distorted emotional background, correcting posture and bad patterns of motor activity, and exercises in progressive muscular relaxation. The training of the speech therapist affords the ideal equipment for treatment; she should be given and should accept the responsibility of dealing with the condition.

## PHYSIOTHERAPY IN NERVOUS DISEASE

No consideration of treatment of neurological conditions would be complete without some discussion of physical methods of treatment. These physical methods are massage, heat treatment, electrical therapy and exercises, remedial and re-educative.

**Massage.**—Massage was the physiotherapist's obsession and dearly has the physiotherapist paid for harbouring it. The devotion to the facile belief in massage prejudiced the whole natural evolution of more useful and rational physiotherapy. A legitimate use of massage is in the treatment of fibrositis. But here the reader is warned. How often is "fibrositis" the first sign of tumour or inflammatory disease? How often is true fibrositis perpetuated by chronic inflammatory disease at a distance—a chronic urinary infection or a cholecystitis? In these instances massage is palliative at the best.

Another point of real significance is the association of fibrositis with neurotic symptoms. Most people can produce pain by sitting stiffly in an awkward position; this being true, it would be surprising if the constant increase in muscular tension, so characteristic of the anxiety state, did not cause pain. In this type of case massage exerts its full psychological effect in the achievement of muscular relaxation.

Massage is of some value in the treatment of those cutaneous vascular disturbances which depend on poverty of movement of a limb. Rubbing will increase blood flow through the skin vessels and may prevent the formation of ulcers and sores. This treatment should be applied only to limbs with a motor defect and not to those with profound disturbance in cutaneous pain sensibility. Massage can make no claim to increase the blood flow through muscle nor to improve any defect in muscle innervation. Blood flow through muscle is a function of its activity in contraction, and the physiotherapist's first concern, when trying to improve the nutrition of atrophic muscle, is, if possible, to make that muscle contract by any means at her disposal.

**Heat.**—Heat can be given in many ways. The infra-red lamp is an adequate source of penetrative heat but its benefits are often purely psychological. Beyond question a hot bath is much more efficient. One can see some justification for the use of the hot wax bath; the thermal capacity of wax is not so high as that of water but wax treatment is kinder to the skin than is prolonged immersion in hot water. Short-wave diathermy is efficient in heating deeper structures but, as a rule, should not be used for increasing cutaneous circulation. Emphasis is laid on the necessity for care in the

selection of cases to be subjected to heat treatment. Trophic lesions with sensory impairment should be largely excluded as the normal axon protective reflex is lost in such cases.

The main use of heat therapy in neurological conditions is to improve cutaneous circulation in parietic limbs, seriously impaired in movement but without sensory change. One subsidiary application of heat therapy may be to induce relaxation of voluntary muscle; this is likely to prove of use in resting the hypertonic muscle of extrapyramidal disease but, at the best, the effect is temporary.

**Electricity in the Treatment of Neurological Conditions.**—Stimulation of muscle by electricity is at once an important and powerful therapeutic agent without which no neurological service can claim full efficiency. Galvanic and Faradic currents are both used. Galvanic stimulation should be used only when Faradic fails to cause a contraction. These modes of stimulation should be employed in cases of weak muscle, atrophic from a lower motor neurone lesion. Their use in any other type of lesion is to be condemned unreservedly for various reasons: the time wasted could be devoted to effective physiotherapy; there is no rational basis for stimulating spastic or rigid muscle, because such muscle already is rendered overactive from pyramidal or extrapyramidal disease; such treatment may make the patient symptomatically worse in the ill-selected case. Good as the results may be in lower motor neurone disorder, not all disease with lower motor neurone signs should be treated in this way. Only when the process offers some hope of regeneration should the treatment be applied. To submit cases of progressive muscular atrophy or of myopathy to electrical stimulation is nonsensical and harmful. Electrical treatment properly administered is time absorbing. Daily stimulation should be attempted and each muscle under treatment should be made to contract ninety times at each session. Such a course makes electrical therapy worth while and that is why wasting time on valueless physiotherapeutic measures is to be condemned. One hint may be given with advantage. When a muscle is very weak the pain of an effective stimulating current may be too great for toleration. Effective stimulation, with reduced current and less pain, is possible if the resistance of the overlying skin is reduced by cleaning and scrubbing with a small nail-brush until red. In a fresh case of anterior poliomyelitis, as soon as electrical stimulation can be tolerated, contractions in weak muscles must be sought daily if the most effective treatment is to be given.

Of other forms of electrical treatment little need be said. Faradic baths may be of some use in the treatment of intrinsic atrophy of the hand as focal stimulation is often difficult and impracticable. Sparking devices and baths with weak sinusoidal currents have less to commend them than the amulets and charms of folklore.

**Exercises.**—Exercises are of first importance in physiotherapy and indeed in medical treatment generally. Graduated exercise of all kinds carry the patient from his early convalescence to full fitness for his former occupation. Although passive movement is scarcely exercise, it is convenient to consider that form of treatment here along with true exercise. True exercise is remedial and re-educative.

**Passive Movement.**—The joints of a paralysed limb should be moved passively through their full range of movement daily. The disadvantages of putting a paralysed muscle on the stretch scarcely count when the benefits

of avoiding secondary fixation are considered. If this treatment is carried out, many a manipulation under anæsthesia will be avoided. Neglected cases will have pain with passive movement, but in such instances a little more movement can be gradually achieved daily without causing the patient undue distress.

*Remedial Exercises.*—These movements are executed by the patient voluntarily at the instance of the physiotherapist. They are divided into various types. Static exercises can be performed even when the patient is encased in plaster. A little instruction and demonstration are needed to show the patient how to brace muscles without moving one part of the body relative to another. These exercises are the clinical equivalents of the isometric contractions of the physiologist. Static exercises can be carried out against resistance applied by the therapist. In cases of inflammatory change or trauma when relative movement of individual parts of the limbs or body might do harm, these static exercises are of great value in preparing the way for the exercises of movement against a load. Thus the aim of the therapist must be to keep the tone of muscle as nearly up to standard as is possible. Not only do these preparatory exercises pave the way for more strenuous activity but they increase metabolism and afford a sense of well-being which would otherwise be denied the immobilised patient.

From the foregoing it can be seen that remedial exercises fall naturally into two classes: those which keep up the general muscular tone and stimulate metabolism; and those which are specifically designed for the treatment of particular muscle groups. Those exercises concerned with the increase of general muscle tone have been described, and in this class breathing exercises which maintain the reserves of the patient throughout illness are also most important. In the second group voluntary movement of specific muscles is encouraged. The efficacy of these measures may be increased when the patient is asked to perform a specific movement in manipulating apparatus specially designed for the particular movement. For example, in peripheral nerve injuries and in polyneuritis, the flexors and extensors of the hand may be made to move effectively by the use of a small apparatus to pump water by compressing and releasing a bulb such as one finds on a sphygmomanometer. The next stage might be the use of spring dumb-bells. For movement of pronation and supination the "wrist-roller" is the appropriate apparatus. For movement of extension and flexion of the foot there is no more effective exercise than bicycle pedalling against an increasing load. For spastic cases, exercises in relaxation are recommended. From prescribed movements the patient passes to use the walking machine. Later, tripod crutches give extra stability and can be manipulated if the arms and shoulder girdle are sound.

One of the greatest developments in physiotherapy has been the use of the Guthrie-Smith apparatus. This consists of a double Balkan beam from which are suspended slings to support the limb under treatment. These slings may be sprung or hung by inextensible cords. By this means many exercises can be performed impossible in an ordinary bed. The whole purpose of the apparatus is to take the load of gravity from the contracting muscle when the muscle is too weak to contract against that force. By suitable posturing of the patient the limbs are slung in the appropriate position for working against the minimum load. Modifications of slinging and springing of slings can be used to put increasing loads on contracting

muscle until full power is regained. The obvious application of this treatment is in poliomyelitis and polyneuritis.

**Re-educative Exercises.**—These exercises are designed to co-ordinate movement when the natural sensory basis for co-ordinate movement is deficient. The patient has no automatic idea where to place his limbs. Use is therefore made of the eyesight to guide the limbs. The patient is trained to walk by sight rather than by reflex and automatic means. With progress in that training, the pathways between vision and locomotion become so canalized as to make the process almost as automatic as it had been when proprioceptive sensibility was intact. Much of the new movement is stilted and jerky and re-education must aim at fostering the normal rhythm of walking. Fraenkel exercises consist of placing the feet on predetermined positions on the floor. The usual apparatus is a mat in the form of a runner with footprints marked on the mat. The patient is instructed to place his feet accurately on the footprints. Music encourages rhythm of movement to produce a more natural gait.

### PHYSIOTHERAPY IN CERTAIN NEUROLOGICAL CONDITIONS

**Tabes Dorsalis.**—Treatment of tabes dorsalis has been considered elsewhere. Instructions have been given as to the specific measures to employ in combating the infective process (see p. 227). Important as these specific measures are, the ultimate success in treatment depends on re-educative exercises. Proprioceptive mechanisms are lost and the function of this mechanism must be replaced by the use of other sensations. Fraenkel's exercises to music are mentioned above and this treatment is essential. Only by assiduous re-education can the tabetic hope to recover facility of movement in walking. Much of this facility may be acquired by himself in the natural course of events, but systematic re-education makes compensation faster and surer. The tragedy of the tabetic so far as reasonable recovery of function is concerned is when his vision is taken away from him because of optic atrophy. Here there is little point in prescribing re-educative exercises because he has then no means of judging the position of his limbs relative to one another and to the surface on which he treads.

**Subacute Combined Degeneration of the Cord.**—The treatment of this disease has been considered elsewhere (see p. 483). Emphasis has been rightly laid on the success of specific measures and the ultimate benefit to the patient of assiduous and constant treatment. Neurological signs, however, seldom disappear completely and often residual symptoms remain. These symptoms are mainly the result of loss of proprioceptive sensibility. Thus, as in the case of tabes dorsalis, the physiotherapist must aim to make the legs obey the eyes when postural sensation is deficient. The means of achieving this end is as in the treatment of tabes dorsalis—Fraenkel's exercises and placing exercises rhythmically performed. By these re-educative exercises residual disability is lessened, limitations imposed by reversible change are narrowed and restoration to useful employment is hastened.

### PHYSICAL TRAINING

Gymnastic exercises are useful in bringing convalescents from certain nervous conditions back to full fitness. Selection of patients for physical training depends on two main factors—the nature of the disease, and the

nature of the patient's former and intended employment. The disease should have a good prognosis and offer reasonable prospect of return to full employment. Although selection for physical training is not necessarily limited by the type of work in which the patient is normally engaged, it will be seen that a higher standard of physical fitness is necessary for the pursuits of a dock labourer than for those of a bank-clerk, unless the latter is an athlete as well. The first point, which depends so much on prognosis, takes cognizance of age and general physical state. The second point is concerned with the load likely to be put on the patient once he returns to a normal way of life.

It is worth while mentioning one or two conditions for which physical training is expedient. Post-concussional states are slow to recover and are an anxiety to patient and physician alike. The sufferer is afraid to exert himself; he is afraid to stoop; his anxieties multiply with the perpetuation of symptoms. Graduated exercises in bed as soon as they can be tolerated start off the physical training: when the patient gets about, exercises in the gymnasium or in the open should avoid stooping at first; later, full fitness can be achieved by vigorous muscular exertions to the command of the instructor. This routine possesses intrinsic value; but more than that, physical training, practised in groups, has a psychological value of no little moment. If the instructor is chosen well the results of treatment will often be astonishing. He can use his knowledge or his instinct to encourage by his own personality or by citing the example of others in the group as a pattern to be copied.

Of equal significance is physical training in cases of sciatica recovering from a herniated disc. Again, exercises in bed are the prelude to extension and rotation exercises in the gymnasium. Flexion exercises are not encouraged and if practised must be of the gentlest kind.

Anterior poliomyelitis in its convalescence requires physical training designed to suit the requirements of the case. The same applies to convalescent cases of infective polyn neuritis—always provided the general physical state permits. Swimming is of immense value in the treatment of many cases with residual palsies whether from anterior poliomyelitis or other cause.

Included in physical training are games. The instructor will organize them according to the requirements of the selected group. If any movements have to be avoided or encouraged the intelligent instructor will select the appropriate game once the rationale of treatment has been explained to him.

### OCCUPATIONAL AND DIVERSIONAL THERAPY

The training of the occupational therapist gives her resource to interest the patient at any stage of convalescence. At first diversion of the patient may be the sole aim of the therapist. As long as the patient is given something to do, something involving the skilled movement of his hands, he will be interested and relieved of much of the boredom of illness. As soon as possible he should be given something useful to make—for example a scarf, by weaving, or a leather article, by cutting and sewing. If there is æsthetic value in the ultimate product, so much the better; the patient has satisfaction in achievement of practical and artistic accomplishment. Occupational therapy is designed mainly for long-term illness, but is of first import-

ance in the treatment of post-traumatic states when head injuries have been sustained. In these states the patient's attention should be engaged in something other than himself as long as he is awake and not engaged in eating or in prescribed resting.

The general effects of occupational therapy are principally psychological, but particular benefits are to be gained when the occupation demands a specific group of movements calculated to restore function in weak muscles. The use of a treadle machine in weakness of the leg and foot muscles is an example of the operative principle of making weak or stiff muscles perform beneficial work almost as if by stealth.

### THE PROTECTED WORKSHOP

Would that the potentialities of the protected workshop were realized. For those severely disabled by nervous disease, condemned to limited activity for the rest of life, unemployable in the open labour market, the protected workshop offers its solution. Illustration by specific examples of protected employment will make its benefits clear. The victims of traumatic paraplegia and anterior poliomyelitis are making electric blankets. They use sewing machines with special controls devised to suit the residual movements in the individual case. An advanced but slowly progressive case of myopathy, who cannot raise his arms above his head and who waddles like a duck, keeps the whole shop supplied by soldering thermostats to element wires; this job he does with an efficiency equal to that of the normal able-bodied man. A simple routine in threading element wires has been learned and is satisfactorily performed by a man dysphasic from a gunshot wound of the head; he has difficulty not merely in expressing himself but in finding his way about his once familiar surroundings. The venture of employing such men is economically sound. This is perhaps of secondary importance to the community as a whole, but it is a fact of the first magnitude in the eyes of the employees.

**The Social Worker.**—No neurological service can be complete or approach its potential usefulness without the social worker. Such workers are available not merely to inquire into the economic dilemmas of the sick but to help them solve the problems of their disabilities. The social worker should see the patient at the hospital, assess the likely problems of the patient's future and follow his career until his resettlement, if that be practicable, in industry. No physician is self-sufficient or knowledgeable enough to appreciate the whole social difficulties of his patients, nor is he qualified to solve the problem for like reasons. He should be ready to put the patients' problems to the social worker when he feels that drugs and doctors must necessarily fail.

J. B. GAYLOR.

## PSYCHOTHERAPY IN GENERAL PRACTICE

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EVERYONE in his heart believes that he is a good psychologist even though he may modestly confine outward expression of that belief to the statement that he is a good judge of character. This is natural, for people are endlessly interested in their own personalities, and find their neighbours almost as fascinating a study. But when an attempt is made to dignify this interest by calling it a science, when experts appear who formulate theories which conflict with popular concepts, then we find great divergence of opinion, ranging from slavish acceptance of the formulations of this school or that to aggressive denial that there is anything in psychology at all. A similar reaction has been observed among members of the medical profession towards psychotherapy—a new and importunate branch of healing which has been engaging the attention and disturbing the minds of doctors and patients to an increasing extent during recent years. To the editors of this book of therapeutics, therefore, it seemed fitting that a section should be devoted to the problems in medical psychology which the practitioner encounters in his daily work.

No space need be devoted to emphasizing the importance of good mental health. It is generally accepted that much unhappiness, industrial inefficiency, social unrest and international strife can be traced to individual maladjustment. Neurotic illnesses are much more common than is suspected, and, according to most authorities, there is, in a third of all cases seeking medical aid, a psychogenic factor which must be recognized in planning treatment. The usual procedure is to refer cases in which psychotherapy seems necessary to the nearest clinic or specialist, but this method can deal with only a small proportion of patients who require treatment. Certainly specialists and clinics are at present too few and far between, but even if they were multiplied many times over there would still be an insufficient number to provide specialist treatment for each patient. Other methods which aim at prevention rather than cure must be found. Provisions already exist in miniature for a broad mental hygiene programme in which child guidance, the inclusion of psychological teaching in the medical curriculum, the training of specialists, the earlier and more active treatment of neuroses and psychoses, and the education of the general public play an important part. Even if these provisions are much more extensive, the burden of treating mild and early cases, the responsibility of eliminating factors which predispose the individual to mental ill-health, must fall on the family physician. No one else has the same opportunity of recognizing and dealing with those intimate environmental and personal conflicts which bring about a disintegration of personality.

That a physician should deem himself capable of undertaking psychotherapy without special training will sound complete heresy to many experts. None the less, it is obvious that the bulk of neurotics will go untreated if they have to depend on the services of specialists, whose exclusive attitude has helped to make the average doctor chary of using even his good common

sense in the handling of these patients. Many of the older practitioners were excellent psychotherapists: they gave mental and emotional attitudes their rightful place in the production and cure of illness. To-day the practitioner has little confidence in his ability to deal with psychogenic factors because he has been taught that only the very learned can presume to practise psychotherapy. One hopes that the introduction of psychology into the medical curriculum will serve not only in emphasizing the importance of this branch of medicine but also in helping to produce doctors who have confidence in their ability to use psychotherapy as part of their armamentarium. Much research, it is true, must still be done, not only by specialists but also by general practitioners themselves, on the methods and techniques which can most usefully be employed in general practice. None the less, certain broad principles can be laid down: the purpose of this article is to outline them, to make certain suggestions as to the conduct of treatment and to indicate the scope and limitations which are operative in general practice.

There is little doubt that, even in the last decade, the attitude of the medical profession has changed radically towards patients who suffer from psychogenic illness. To begin with, these disorders have been given a place in reality; patients are no longer told to the same extent that "there is nothing the matter with them except nerves," and, therefore, they no longer leave the doctor's consulting room with a feeling, half of shame and unworthiness and half of fear that their nerves—those mysterious and awesome structures of which they know so little and conjecture so much—are in some way upset or diseased. Even to be told that their trouble is mental rather than physical is a tremendous relief to those frightened and unfortunate people. True, they may protest vigorously against such a diagnosis, but their defence is healthy in comparison with the furtive defiance with which they greet the verdict that they are not ill at all. Their senses, their feelings and thoughts compel them to recognize that something *is* wrong, and naturally they prefer to persuade themselves and their doctors that that something is a physical malfunction. If the liver is out of order, cannot one swallow comforting and magical pills? If the stomach is upset, are there not well-known powders to be bought? If anything is wrong with the body it can hardly be one's own fault and there need be no turning over of painful memories, no stirring of the dark and inmost recesses of thought, no facing of unpleasant facts, no thinking that life is too difficult.

Patients thus come to the doctor consciously in misery, consciously eager to get better, but unconsciously determined to do everything in their power to remain ill. Indeed "one may say that they constitute the only condition where the patient comes for help to sustain the disease and resists every effort to cure it."<sup>1</sup> Now when the doctor realizes that the patient, far from wishing to get well, hopes to use him as a means of retaining his symptoms, he is inclined to be filled with righteous indignation and to eject him with harsh words. But no matter how obvious it is that the neurotic wishes to remain ill, the doctor should remember that the patient will be the last to realize it; that, indeed, his symptoms would be of no use to him did he understand their purpose. Nor must the doctor suddenly blurt out this fact, for, if he does, the patient will either frankly disbelieve him and seek a more naïve doctor, or will experience a collapse which may end in suicide.

<sup>1</sup> Jones, Ernest, *Brit. Med. Jour.* (1938), 1, 1354.



For neurotic symptoms are purposive, in that they defend the patient against something that he dare not face. The patient has come to the doctor for help only because he feels that his protective mechanisms are breaking down and because a corresponding degree of anxiety threatens to overwhelm him. Take away those defences suddenly and disaster will follow. Of course it is a great temptation to make a dramatic cure, but one which the doctor will be more able to resist if he remembers that a neurotic illness is often the result of a lifelong maladjustment, and that one cannot expect to change a man's character, personality and mode of life all in five minutes. The hysteric may seem to be the obvious exception; for paralyses, anæsthesias and other conversion symptoms may be cured suddenly and with no obvious harm to the patient; but these dramatic cures, temporarily satisfying though they may be to the physician, the patient and the anxious relatives, are seldom the end of the neurosis. In fact, the sudden cure is only harmless when another symptom appears to make good the patient's defences. Only by a slow process of reintegration can the patient be brought to see what his symptoms mean and how he may safely discard them for more healthy and permissible mechanisms. It is as if the patient had been treed by a lion and realizes that the tree he has climbed is liable to fall at any minute. A few yards away is a sturdy tree, which would harbour the patient in complete safety, but he is afraid to cross the gap, and comes to the doctor hoping, not that he will help him over the dangerous ground but that he will chase the lion away or tell him that his tree is perfectly safe. Great care is needed in persuading the patient to leave his insecure perch and pass the lion on his way to safety. This analogy is too full of generalizations to bear close scrutiny, but it contains a modicum of truth and is readily understood by patients.

The patient, then, comes to his doctor hoping that he will confirm his dear wish that his symptoms are due to heart disorder, or what you will, and must gently be shown that this is far from the truth. But an even more curious attitude on the part of the doctor must be noted, as Jones points out,<sup>1</sup> which is that the doctor and the patient may both wish to avoid a cure. Both are human beings and both use defensive mechanisms against their unconscious fears. Neither wishes to disturb the dark recesses of the unconscious, for who knows what horrors may emerge if the barricades are torn down. Whether, as Jones implies, this is true of all members of the medical profession or not, it certainly is true in certain cases. Consider the patient who was injured at his work and who later developed vertigo and other very obviously hysterical symptoms. Going to his doctor he asked whether his symptoms were due to head injury. "Well," said the doctor, "you never know with head injuries. Your head is like an orange; you can squeeze the inside of it into pulp and the outside looks quite undamaged. The outside of your head looks all right." Surely the doctor in this instance was at one with the patient in wishing that there were some organic lesion to account for the symptoms puzzling to him and frightening to the patient. It is much easier to think physiologically rather than psychologically (one has only to read the journals purporting to be devoted to psychiatry to realize this); it is difficult to think of man being a psychobiological organism rather than a mind and a body only remotely related. We shrink away from the emotions and their power, encourage the patient to make light

<sup>1</sup> Jones, Ernest, *Brit. Med. Jour.* (1938), 1, 1354.

of his symptoms, urge him to "pull himself together," to play golf, to get married and, most shamefully of all, to "use his will-power." Would that some prophet would cry from the house-tops, "Will is the organized self in action." How can a neurotic use will-power when his self is disorganized?

How then can the physician avoid his human tendency to be blind to psychogenic factors in illness? Jones has suggested that only "real" psycho-analysts (those belonging to the Freudian school) can avoid this pitfall because they have been analysed themselves. It should be pointed out that such an analysis takes about four years, is very expensive and is obviously open only to a minute percentage of medical practitioners. In addition, he would have us believe that psycho-analysis is the only form of psychotherapy of any value. Those of us, however, who are familiar with psycho-analytic thought, are undisturbed by such statements because they are so obviously determined by the lack of insight into their own unconscious processes which so many disciples of Freud show. It is true that the doctor who wishes to practise psychotherapy must be prepared "to face calmly the contents of his own unconscious mind and to have personal experience of resolving the conflicts and anxieties of it."<sup>1</sup> This can be done (one is tempted to add, better) without undergoing an orthodox Freudian analysis.

Now while it is impossible, and indeed inadvisable, in our opinion, for the majority of doctors to be analysed, it is imperative that they should all be alive to the importance of the mental processes in all disease. They must have, as Yellowlees says, "a living interest" in this aspect of medical knowledge. This they should acquire partly from teaching at their medical school, partly by reading, and most of all by experience. The really great physicians are noted chiefly for their deep understanding of human nature and for their sympathy with its frailties. The family doctor has, in particular, an unrivalled opportunity to study not only the individual but his relations to his family, his friends, his work and his recreations. Often he has the privilege of watching him develop from birth to manhood and, unless he be particularly blind, he should be in a unique position to guide him through some, at least, of the difficulties of life. It should be the ambition of every doctor to be the counsellor of his patients both when they are physically ill and when they are in difficulties of a more subtle but perhaps more important character. Of these difficulties there are perhaps three which are most often encountered—parent-child relationships, the adjustment of the sexual instinct and the attitude of the patient to disease. These three subjects are of vast importance in maintaining good mental health, and every physician should have some knowledge of them.

## GENERAL PSYCHOGENIC FACTORS

### PARENT-CHILD RELATIONSHIPS

Precipitating factors are found in most neuroses—the death of a relative, loss of employment, an accident, financial difficulty and misfortunes of many kinds are plain for all to see, but knowledge of them is of little comfort to the patient. The physician must look for more deeply hidden ætiological factors which render the patient potentially neurotic, and which the current difficulty has, by association, stimulated into activity. These latent factors

<sup>1</sup> Jones, Ernest, *Brit. Med. Jour.* (1938), 1, 1354.

are the conflicts, inevitable in the process of early development, which have remained unresolved. The physician who has a working knowledge of these developmental errors should, through his close association with the family life of his patients, be able to do something to prevent their occurrence or to understand their ætiological significance in later life. Some understanding of the problems of child psychology can be gained by reading such books as "The Inner World of Childhood,"<sup>1</sup> "The Psychoanalytic Study of the Family,"<sup>2</sup> "The Mind in Daily Life,"<sup>3</sup> "Bringing Up Children,"<sup>4</sup> etc., but such study can only be made vital by personal observation of children themselves.

The student of early development will quickly realize that, even in ideal circumstances, the child has many conflicts to resolve during his first few years of life, and that the neuroses of anxiety, aggression, temper-tantrums, feeding and excretory difficulties are common to all children. The infant has to solve conflicts between instinctive reactions and behaviour which is socially acceptable. In those formative years he must pass from a state of primitive savagery to a stage of cultural and social development which mankind has taken untold centuries to attain. Here it is not possible to consider these conflicts in detail, but it is important to note that development takes place smoothly only under ideal circumstances. Either a faulty endowment or a harmful environment, or a combination of the two, will cause a breakdown in childhood or later life. What surprises us is the capacity for adaption to difficulties, the resilience against neuroses and psychoses which the child displays. We understand little of and can do little with a poor hereditary endowment, but we can manipulate the environment so as to relieve undue strain. Study of neuroses in childhood has shown that there are certain conditions for which the child craves in order to make the solving of these inevitable inner conflicts possible, and that the most important is undoubtedly what child psychologists call *security*. By security they mean that the child absorbs from his parents a certain degree of affection, that he should have discipline which can control impulses too strong for himself to deal with, that there should be continuity of home life to compensate for the bewildering changes he experiences within himself, and that the adults around him should demonstrate that they have the power to regulate their own thoughts and feelings. And, lest we become too much absorbed in theory, we should note that these are just the things which wise parents do give their children intuitively.

The child also needs to *play*, for childhood is a period of experiment, trial and preparation. Through play the child is able to dispel his fears. Simple materials are used by the child to create situations of which he is afraid inwardly but over which he feels that he has mastery in a symbolic form. Again and again the child will go through such a performance until his inner fears have found surcease. This phenomenon forms the basis of the most recent technique for dealing with neuroses in childhood.

As an example, we may refer to the case of a child, aged four years, who hated and feared her mother; she had good reason for these feelings, for her mother was most unstable and unwise in the way she treated her. The child,

however, knew, perhaps intuitively, perhaps from experience, that it would be unwise to show her antagonism openly, but showed her feelings in the following manner. She was given a family of dolls to play with and at first paid no attention to the mother doll. After playing with the others for some time, she suddenly picked up the "mother" and, with an expression of ferocity, twisted its head off. On another occasion she made a drawing of a woman and said that this was her mother. When the drawing was completed she regarded it thoughtfully for a time and then asked, "Do people with blue faces die?" On being told that cyanosis generally heralded death, she seized a blue pencil and carefully coloured her mother's face. Such behaviour is common enough among young children, and reminds us of the custom prevalent in primitive civilizations of making a wax or clay image of an enemy and sticking pins into it in the belief that the enemy will thereby suffer harm. It should be added that the child mentioned above seemed relieved by the symbolic expression of her feelings and became more amenable to her real mother thereafter.

Again a child, to develop normally, must have *work* suitable to his intellectual capacity and stage of development. The intellectual faculties are capable of balancing and controlling the emotions and the child who has no outlet in work becomes a prey to uncontrolled impulses. Work to the infant means the learning of bodily skills, walking, talking and the manipulation of external materials; to the older child it means formal education. Hence Moodie's dictum, "Early and efficient teaching in the fundamental subjects of reading, writing and arithmetic is the corner-stone of mental hygiene in children."

Without these fundamental needs of security, play and work, and all that they imply, the child tends to develop a fear of growing up. He is, therefore, potentially vulnerable either during childhood or during adolescence or while facing any of the major life adjustments. Faced with any situation which calls for an integrated and stable personality he will tend to regress to an infantile mode of reaction. And now we see the necessity of uncovering those repressed and unresolved conflicts of childhood when attempting to cure a neurosis in an adult. Unfortunately these conflicts are often deeply buried in the unconscious by the time the individual has reached maturity and their elucidation may be beyond the skill of anyone but an expert, but the general practitioner can do much to prevent their occurrence by ensuring that the fundamental needs mentioned above are supplied as far as possible, and in certain cases he may be able to deal with them in later life.

### THE ADJUSTMENT OF THE SEXUAL INSTINCT

Probably Freud's discovery of the important part which the sexual instinct plays in the formation of the neurotic's reactions, and of the great influence which this innate force plays in the thoughts, feelings and behaviour of every individual, startled the world more than any other piece of research. His theory lit up the comfortable Victorian world like a flame from the nether regions, and indeed many believed that he was inspired by the dark forces of evil. We are not concerned here with the complexity of Freudian psychology, but there are certain simple facts which have emerged which are of vital importance in the ætiology of the neuroses and

which should be known to every medical practitioner. First of all, one must remember that the sexual instinct is a natural force which causes no trouble when given natural outlet. Malinowski<sup>1</sup> has shown that in a primitive tribe where sex is allowed to develop freely there is no such thing as a sexual neurosis. Only in a civilization like our own, where there are so many social and moral taboos, and where there is such an acute feeling of guilt attached to this instinct, does it assume undue significance and power. It is noteworthy that sexual factors are less frequently found to be ætiologically important in centres like London and in the U.S.A., with their less exacting standards, than in certain provincial districts where there are more rigid codes. Significant, also, is the fact that sexual troubles are more often found in the professional classes, where economic factors delay marriage long after the individual has reached maturity, than in the labouring classes, where the individual attains his maximum earning capacity about maturity, or among the rich, where there is no economic bar to marriage. Sex, therefore, is a force with which the medical profession must reckon only when it is dammed up.

Again, one must realize that the child has a sexual life of its own, but naturally it differs widely from adult sexuality. Much harm is caused by adults who regard the manifestations of sexual activity in children as they would regard similar activity among their coevals. Here the adult is projecting his own knowledge and feelings on to the child and the child suffers feelings of guilt which may colour his attitude to sex all his life. This is illustrated clearly with regard to masturbation. Almost all children masturbate at some time or another, but masturbation in a baby of six months cannot be sexual in the adult sense. In young children and babies autoerotic practices are indulged in mainly for the sake of sensual gratification and are allied to behaviour disorders like thumb-sucking, and should be treated as such. It is practised chiefly by children who are bored, or insecure, or in pain, and appropriate adjustment can be made if steps are taken before a habit is formed. On no account should the child be made to feel guilty. Sexual curiosity is also a very real thing in children, but again it is not dangerous, provided parents are able to satisfy that desire for knowledge in a natural and unemotional manner. If uninstructed, they will gain their knowledge in an undesirable way, or, by brooding over it, conjure up harmful concepts, and either way will spoil their chances of attaining a healthy attitude in later life. Much harm is done because so many parents have themselves feelings of guilt about sex, which are intensified when they try to answer their children's questions. The children sense this and get the impression that there is something shameful about sex, and so the vicious circle is perpetuated. It should be remembered, too, that children can suffer anxiety or have their sexual feelings prematurely aroused by observation and misinterpretation of sexual behaviour on the part of adults around them.

Masturbation in adolescence must be regarded as something different from autoeroticism in children. Our experience shows that it is still necessary to warn doctors that this practice, *per se*, does no physical or mental harm. The harm comes from the feeling of guilt which follows the practice. Masturbation does not weaken the patient, but the emotional disturbance does, especially if the patient has been told so by his doctor, his parents or some would-be counsellor. Most pernicious of all are books like the "Family

<sup>1</sup> Malinowski, B., "The Sexual Life of Savages in Northwest Melanesia." Routledge, 1929.

Physician" or those pseudo-medical, pseudo-religious books<sup>1</sup> which promise to the masturbator as many ills, from tuberculosis of the spine to insanity, as certain proprietary pills claim to cure. What must be realized is that the adolescent masturbator is already overburdened with guilt and must be relieved of it before he can conquer the habit. "Nor must it be imagined," as Brill says, "that robbing masturbation of its horrors encourages its practice. On the contrary, I have found that as long as patients dread it they masturbate twice as much as when they become convinced that it has none of its former supposed horrors."<sup>2</sup>

We cannot here discuss in any detail the part which sexual maladjustments play in the neuroses of adult life, but mention must be made of the influence which lack of sexual satisfaction plays in the production of diseases peculiar to women. Gynæcologists are becoming more and more aware that operations performed for the relief of pelvic pain are, in many cases, the wrong treatment. Unfortunately, it is often easier to perform an operation than to discover why the patient is having lower abdominal pain. Such patients are most resistant to a psychogenic interpretation of their condition, partly because they find it difficult to believe that the "real" pain they suffer can have a mental origin, partly because their modesty makes them unwilling to discuss sexual problems. But to the family doctor who knows the patient, the husband and the mode of upbringing, the trouble should be obvious enough.

There are two main types of patients who suffer from pelvic disturbances of a psychological nature. The first is the spinster who, all her life, has been starved emotionally, but whose vague hope, that some day she will marry, maintains fair stability until something makes her realize the poverty of her emotional life. This realization may be activated by the death of a relative, by an unrequited love affair, or merely because advancing age compels her to recognize that soon her hope of romance can no longer be maintained. The pelvic pain expresses, in a symbolic manner, the patient's inability or disinclination to face the bitter fact that she cannot attain her biological end in life. The second, and much more common type, is the married woman who has not obtained sexual satisfaction from her husband. It is true that a high percentage of married women never obtain enjoyment or satisfaction from coitus, yet they do not suffer from psychogenic pain. These women have never had cause to believe that any satisfaction could be obtained from intercourse; they think of it simply as a somewhat unpleasant duty towards their husbands which they must perform with as good grace as possible. But let them once experience extra-marital satisfaction and trouble soon begins. Here is a typical history. A woman of thirty-seven suffered from such acute pelvic discomfort that a gynæcologist performed a hysterectomy. The uterus was successfully removed but the patient complained, during the post-operative period, of headaches, depression, sleeplessness, and weakness, which could not be accounted for on a physical basis. Accordingly a psychiatrist was consulted who elicited the following history: The patient was illegitimate and had married mainly to obtain social status. Her parents-in-law did little to conceal their disapproval of the match and, as they lived in the same town, were able to

<sup>1</sup> Good examples are "Onania or the Heinous Sin of Self-pollution," an anonymous work published in the eighteenth century, and "Instruction for New Confessors," Salvatori, 1885.

<sup>2</sup> Brill, A. A., "Psychoanalysis," p. 34. Sanders, 1913.

interfere persistently with her domestic affairs. The husband was inconsiderate and impulsive about intercourse and tended to neglect her in other ways. Her health remained fairly good until she fell so deeply in love with another man that she considered leaving her husband and child. Because her religion forbade this, she decided on the compromise of illicit week-ends, in the course of which she first experienced sexual satisfaction. Then her lover, becoming tired of her, departed to India, and soon the patient began to experience acute pelvic pain, for which the hysterectomy was later performed. Both because no organic disease was found in the uterus and from the psychological history, one can legitimately infer that the pain was defensive, expressing as it did her bitterness at the loss of sexual satisfaction from her lover and acting as a subconscious excuse against intimate relations with her husband. When the operation removed what she consciously believed to be the cause of her pain, she had to develop other symptoms which would subserve the same ends. These symptoms were entirely relieved by psychotherapy, and the patient became much more happy in her marital life.

### THE ATTITUDE OF THE PATIENT TO DISEASE

Disease is perhaps the most dramatic thing which occurs in the life of the average person; it is little wonder, therefore, that he should take so much interest in it when it does occur. We do not often reflect that physiologically and psychologically our bodies and minds are designed to encounter and deal with considerable dangers in the external world. Our ancestors were constantly meeting danger and reacting to it in an appropriate manner, but now external dangers are rarely encountered. There are occasional wars or threats of war; there is the danger of traffic but, on the whole, the vast majority of people lead a humdrum existence with no call to feel frightened: but we still have within us a strong instinct of self-preservation which, in the absence of external outlet, tends to be introjected in the form of fears and obsessions about our bodily health. There are, of course, outlets familiar to all; books on crime and horror have immense sales; plays and pictures of the gangster type are very popular; speedway racing and other dangerous sports provide vicarious satisfaction. These things certainly play some part in providing an external outlet for this instinct. The man of to-day will describe his last illness or operation with as much relish and wealth of dramatic detail as the warrior would relate the tale of his latest battle, the explorer his most recent adventure. This is an aspect of disease which has attracted little attention in medical circles, yet surely the doctor's first question on seeing a patient should be, "What attitude does this patient take towards his illness?" His chance of effecting a cure would be much greater if he could allay mental distress, soothe fear and discourage the pleasure and satisfaction which some people get from being ill.

**Hysteria.**—A good example of a maladjusted attitude is found in the so-called traumatic hysterias. The very name shows that there is much loose thinking in medical as well as legal circles about such cases, for the actual injury does not produce the neurosis; the patient's attitude towards the events after the accident is the real cause. Compensation hysteria would be a more accurate term, for, almost always, the patient is receiving a weekly benefit or attempting to obtain a lump sum. Hysteria does not

follow injuries received in sport or when the patient can derive no benefit. Both doctors and lawyers are now beginning to realize that many of these disorders are psychological, but this knowledge does not seem to make them any wiser in their handling of them. Judges and juries are inclined to be either sentimental in their estimate of the mental suffering which the patient has experienced, or mistaken in thinking that hysteria is something like malingering.

Whenever a doctor is called upon to examine a patient suffering from an injury for which compensation may be sought, he should keep in mind the possibility that the symptoms are (1) purely organic in origin; (2) hysterical, *i.e.*, unconsciously determined; (3) the result of malingering, *i.e.*, consciously determined. Certain cases will present a combination of organic and functional elements or organic and malingering, but it is uncommon to find a combination of hysteria and malingering. Such a differential diagnosis is never easy. Physical examination should be as thorough as possible and should be supported by laboratory tests where necessary, the main object being to determine whether the symptoms are of the nature and extent to be expected from the injury. If the symptoms cannot be explained on physical grounds then one must consider whether a functional element is present. Here one must differentiate between an unconsciously determined hysteria and a consciously determined state of malingering. In making a differential diagnosis between those two conditions one should remember that hysteria is a definite disease characterized by certain positive features.<sup>1</sup> These are:—

1. It must prove negative to all clinical and laboratory investigation.
2. There must be found a positive psychogenic basis.
3. The psychogenic factors must bear direct relation to the patient's symptoms.
4. In view of the fact that a psychoneurosis, however suddenly it may appear, has always a background in time, there must be discovered in the life-history of the patient a neurotic trend which, it may be found, has been responsible in the past for the production of subjective states analogous to those under investigation.

*Malingering*, on the other hand, is characterized by:—

1. A tendency to overact the part. This enables the examiner to devise certain simple pitfalls into which the malingerer readily falls. A simulated anæsthesia, for example, can usually be detected by the response to Faradism with a wire brush.
2. The subject is prone to produce any symptom which the examiner appears to expect. This must not be confused with the suggestibility of the hysteric.
3. The malingerer dislikes being examined and is uneasy during the process; the hysteric, on the other hand, delights in examinations and openly shows his satisfaction in the minute investigation of his condition.
4. It is rare for a malingerer to feign new symptoms, rather he pretends that existing symptoms still persist. The hysteric, on the other hand, rarely is content with the *status quo*, and produces a great number of typically hysterical symptoms. Often, indeed, the



hysteric will state that his injury has completely healed, but that he has palpitations, vertigo, feelings of pressure in the head, anæsthesias of the glove or stocking type, etc. If the malingerer does produce symptoms *de novo*, they are generally of a dramatic, artificial and exaggerated type.

5. The malingerer plays his rôle only when observed.

So far as treatment of compensation cases is concerned, the mistake is too often made of thinking that a hysterical condition will clear up when a settlement is made. This is by no means true, especially as many cases drag on for months or years: symptoms become fixed reactions and the patient is thus "hoist with his own petard." Therefore, having decided that there is, or may be, a psychogenic element, the doctor should immediately begin psychotherapy. This consists, in the first place, of warning the patient that the worry, disappointment and self-deception, which inevitably occurs, will delay and perhaps prevent recovery. If, in short, the patient goes on with his case, he should do so with full knowledge of what harm may befall him. It may even be necessary to warn a patient, who has got into the hands of an unscrupulous lawyer, that he, the patient, will not benefit as much as his legal adviser if and when compensation is paid. It should be added that even reputable lawyers, who lack medical knowledge, may fail to recognize that human beings are only too eager to exaggerate illness, especially if they are rewarded for doing so. Illness is obviously preferable to work if the former has a maximum of incapacity and a minimum of pain, and if the latter is monotonous and distasteful. Continuing his treatment, the doctor should try to get the patient to realize that his symptoms, real enough to himself, are in the main due to anxiety and not to the original injury. To convince the patient that this is so is by no means easy, and much depends on the physician's own attitude. He must show the patient that he regards functional symptoms as being just as important and worthy of treatment as symptoms arising from organic causes, and must show no sign of despising the patient for having them. Having gained the patient's sympathy, the doctor can then go over the history of the illness chronologically, pointing out which symptoms were directly the result of injury and which arose from the patient's own attitude. This procedure of piecing together the temporal relationships between symptoms and psychological disturbance gives the patient an entirely new attitude towards his illness and is of considerable value in treatment. Further, the patient should be urged to get back to work as soon as possible; he should, however, be warned that he may have a return of his symptoms when he starts work, but this should only serve to convince him that his symptoms are of mental origin and that they will gradually disappear if he continues with his work. He can be warned that each day he delays will make his symptoms worse, and that no sum of money will compensate for the mental pain he will inevitably suffer.

It should be remembered that the law, as it stands, encourages psychogenic illness because of the delay which takes place before cases are settled, and further, because the patient finds that his right to compensation may be prejudiced by accepting employment before his claim is settled. Therefore, doctor and solicitor should combine in making every effort to settle the compensation case with as little delay as possible.

Before passing from this section dealing with the neurotic reactions which may arise from the patient's attitude towards illness, mention must be made of certain almost traditional fears. A simple example is the fear which many women have of parturition. No doubt this is largely dependent upon the exaggerated accounts of the pain and dangers of child-birth which is passed from mother to daughter, and, of late, the press publicity, which has been given to maternal mortality, has not helped matters. An interesting experiment is being carried out by Miss Margaret Morris, who has designed courses of exercises which tell the patient what to expect during child-birth, and what she can do to help. These exercises make the patient interested in the process of parturition and do much to dispel fear. An obstetrician has reported a case whose first two children were delivered by forceps with great pain and difficulty; during the next pregnancy Margaret Morris exercises were practised and the patient became so proud of her skill that she refused all anaesthetics and delivered the child unaided and without difficulty.

Another traditional fear is the dread of cancer. Whole families become hypochondriacal because of a death certificate containing the terrifying words, so much so indeed that some doctors refuse to put malignancy as a cause of death. Doctors should be at pains to point out that there is no evidence to support the common belief that malignant disorder is hereditary. The following history will indicate the insidiousness of this fear: An exceptionally intelligent man, deprived of education by circumstances, developed a duodenal ulcer, as a result of which he experienced a long period of unemployment. He developed toothache and had some teeth extracted, but, no doubt because a dental student did the extraction, his jaw was painful for a day or two afterwards and he asked his doctor for a line to see a dental surgeon at the local hospital. When the doctor made out the line he put, in the space for "conditions for which the patient has already received treatment," carcinoma of the duodenum. The patient, reading this, immediately thought that the pain in his jaw was due to secondary deposits, for, to relieve the boredom of unemployment, he had been reading about cancer in medical textbooks in the public library. It was little wonder that, despite reassurance that there was nothing wrong with his teeth, his pain grew steadily worse and did not disappear until the psychogenic basis of it had been explained to him.

## DIFFERENTIAL DIAGNOSIS

Many practitioners find difficulty in making a differential diagnosis between insanity and neurosis. Certainly there are early stages in which even specialists can be baffled, but the vast majority of cases present no difficulty. It is helpful to have in mind a simplified classification of the psychoses for, if one excludes the organic-reaction types such as G.P.I., senile dementia, etc., distinguished by their concomitant physical signs, one is left with only three main types. These are (1) schizophrenia with its delusions, hallucinations, bizarre behaviour and signs that the patient has made a retreat from reality; (2) paranoia, a rare condition in its pure form, with systematized delusions of persecution and otherwise well-preserved personality; and (3) the manic-depressive type where the main symptom is an elation or depression of mood. The neuroses can be classified as

neurasthenia, anxiety states, hysteria and obsessional neuroses; the patient suffering from any one of these conditions is commonly called a neurotic. Neurasthenia is much the most difficult to diagnose, for it may be confused with the prodromal stages of G.P.I. Beware of the middle-aged man with no history of previous breakdown, who feels constantly tired, and who complains that he is becoming less efficient. He may have no physical signs, yet his symptoms may be due to the elusive spirochaeta, and the true diagnosis may have to be made in the clinical laboratory. Secondly, a diagnostic distinction between neurasthenia and a mild psychotic depression is important, for the former has little risk of suicide whereas in the latter it constitutes the main problem of treatment. The cardinal symptom of neurasthenia is excessive fatigue, but the patient's emotional reactions are most active; a neurasthenic is always tired except when he is talking about himself, and he is loud in his complaint of the handicap from which he suffers. He is eager to work and take an active interest in outside affairs and bewails his inability to do so. The depressed patient, on the other hand, centres his slow thoughts on his own troubles, the outside world means little to him, and he makes no complaint of the limitations which his condition imposes. The risk of suicide is always present with patients showing these symptoms, whether they express a desire to end their lives or not. But it should be remembered that neurotics also may allow themselves to be driven to suicide. This is particularly true of cases of long standing which have their defensive symptoms suddenly removed. If, for instance, a patient has defended himself from some fear by believing that he has a diseased heart and one proves that his heart is sound, he may find his inner adjustment so disorganized, and his distress so great, that he may end his life rather than face it. The sudden cessation of long-standing fears may then be a danger sign. This is understandable enough if one remembers the parable of the man who swept seven devils from his house but neglected to put anything in their place, and seven other devils more terrible than the first entered in and took possession, so that his last state was worse than his first.

## PROCEDURES IN TREATMENT

There is a tendency to attach an unnecessary degree of mystery to psychological treatment of the neuroses. Many doctors find themselves baffled and ill at ease when faced with a psychogenic illness; they have a feeling of helplessness and are constantly asking themselves what they should do. They long for some active procedure and are, of course, encouraged in this by the patient. Here one should remember the very natural unconscious reluctance, mentioned above, of both doctor and patient to uncover the roots of the trouble, no matter how superficial these may be. In a large proportion of cases met with in general practice, there is no need to go deeply into unconscious mechanisms, for the trouble is fairly obvious to an inquiring and unprejudiced mind. Another point is that the physician must not feel that he is doing nothing because he is giving no active physical treatment. The truth is that everything one does with a neurotic is treatment, and the more passive one is, that is, the more one encourages the patient to work out his own problems, the better results one gets. One must have something of the attitude of the angler who is perfectly confident

that he is going to catch an enormous fish but is quite happy with his day's sport if he lands nothing. Above all, avoid the temptation of using too much explicit suggestion, do not, for example, use methods of treatment such as tonics which have no effect on the root causes of the trouble. Implicit suggestion is unavoidable and the patient should feel your calm certainty that what you are doing is the correct and only treatment, but you should not encourage that part of him which wants you to say that there is nothing wrong, nothing to fear, and that he, therefore, need not bother himself to face his troubles.

In making a diagnosis of a psychogenic disorder the physician must make quite certain that there is no organic disturbance. This involves a most complete physical examination, supported, if necessary, by laboratory procedures and the advice of specialists. Of course the presence of physical disease does not exclude the possibility that the main trouble is psychological. Autointoxications of various kinds are often present and must receive the appropriate treatment, but the physician should not deceive himself that, in so doing, he is treating the neurosis itself, nor should he allow the patient to think so. Another point is that a neurosis cannot be diagnosed by exclusion. It is not permissible to say that the trouble is psychological just because one has found no organic cause. There are, in fact, some cases in which neither cause can be found, and here one must admit that one has reached the outposts of one's knowledge, and one must await the development of additional signs and symptoms. Having satisfied oneself that no organic disturbance can account for the symptoms, one must tell the patient so, and make sure that there are no doubts left in his mind. Such doubts may, in the course of treatment, recur, but the physician should not re-examine the patient physically unless he is satisfied that there is good cause for doing so. This is one of the reasons why the original examination should be thorough, because certain patients are sure to produce symptoms in any part of the body omitted.

Having assured the patient that there is nothing wrong physically, one must explain that the cause is psychological, illustrating the power of mind over body by simple examples, or, better still, by citing case histories of a similar nature. Examples of the former should be confined to bodily reactions in response to emotional disturbance which are likely to have come within the patient's own experience. Most people have experienced fear or disgust and yet the dramatic bodily changes in response to these emotions are not considered strange or terrifying. The physician should try to show the patient that his symptoms are merely responses of a similar nature which indicate that his body is working normally and not, as he imagines, pathologically. The patient should be asked to think over his own experience from this point of view and an appointment should be made for next day, or soon after, when the physician can conveniently spare at least an hour. Most busy practitioners may feel that they cannot possibly spare so much time on one case, but it is better to allow the patient to talk himself out at one sitting than have him pester you day after day for short periods. If, at this second session, no indication is given as to where the trouble lies, it is probable either that the patient is suffering from an incipient psychosis, or that the case is one for a specialist, or, indeed, that there is no psychological basis at all.

If, however, it is clear to the physician or to the patient (though with

the latter this is seldom the case) that the symptoms have a purpose, then subsequent interviews must be arranged. In most cases it is best to see the patient once a week for a month or six weeks and if he is not very much better by that time, or if the physician does not know on what lines to proceed, then a specialist should be consulted. Above all, remember that no rash or hurried interpretation should be given to the patient of the meaning of his symptoms. The physician should interpret mainly mechanisms with which the patient is not familiar, always illustrating from normal reactions or from other cases; otherwise he should confine himself to criticizing or agreeing with the patient's own reading of his case. This can be illustrated by the case of a young man who complained of weakness, palpitation and precordial pain. He explained that he had for many years indulged in masturbation yet enjoyed good health. Immediately prior to the onset of symptoms he had read about the harm which the habit did and, greatly terrified, had stopped it. He attributed his symptoms to the delayed effects of masturbation. Here the physician's function was to point out that his symptoms were due partly to his anxiety and feeling of guilt and partly to the emotional disturbance implicit in the giving up of an act which had served as a relief to the tension of his sexual urges, and not, as he thought, to the harmful effects of masturbation *per se*.

None the less, there are two main lines of inquiry which the physician must keep in mind. The first is simply that a detailed, chronological history of the onset and course of the illness should be gradually built up. This will enable both doctor and patient to see the connection between circumstances and events and the onset of symptoms. The patient will then come to understand the defensive nature of his symptoms and, further, he will realize that there is no longer any need so to protect himself. The history of a patient whose symptoms disappeared in three interviews will illustrate this. He was a man of thirty-seven who, five years previously, had given up an important appointment in the city because he suffered from vehicle sickness and fear of traffic, and had buried himself in a small country town in an unimportant job. When the patient, an only child, was ten, his father died and, by heroic measures, his mother continued his education. He grew up with an intense admiration for his mother and dreamed of the time when he, a successful business man—a captain of industry—would justify her sacrifices and give her a life of ease and luxury. But success of this type is not too easily attained, and, at the age of thirty, he found himself leading a monastic existence in order to send every penny to his mother and still far from being able to marry, or even to live in comfort, far less support his mother. His mother then made a further sacrifice by remarrying, for she saw that her son would miss all the reasonable satisfactions of life in his attempt to pay her back. The patient, suddenly stripped of his former purpose in life, for a time led a life of what to him was riotous living, that is, he moved into comfortable lodgings, no longer stinted his meals, went occasionally to the theatre, and oh, wicked extravagance, took up golf! He even got married himself and, for a time, was quite happy. Then, to his dismay, he found that his step-father, a man whom he disliked and feared, was ill-treating his mother. No doubt because of his anxiety he then made a foolish mistake in his work and was threatened with dismissal. The following morning he became violently sick in the Tube going to work and his doctor foolishly sent him away for three months' "complete

rest." When he attempted to return to work, he was a confirmed neurotic.

It may be asked why the doctor is considered to have acted foolishly in sending the patient away for a complete rest. The so-called rest cure has been one of the recognized methods of treating nervous disorders from time immemorial and reached its epitome in the Weir Mitchell régime, but very little thought is required to see that rest without active psychological treatment is the worst possible therapy. It is, in fact, an admission that nothing can be done for the patient, and is analogous to immobilizing a patient with an acute abdomen and refusing to operate. The patient is sent away from his habitual occupations, social outlets and work, factors which are of the greatest importance in supporting him against his inner complexes, to a place where he will have nothing to do except struggle with his disturbed emotions and his unresolved mental conflicts. Such a procedure too often results in the symptoms becoming a more habitual reaction than ever. The physician should therefore think very seriously before he takes such an important step as certifying a neurotic as unfit for work. He must evaluate the ætiological factors carefully, for it is only when the environmental influences can be held responsible or mainly responsible for the patient's illness that the cessation of work should be recommended. There are cases, of course, when the patient is ill mainly because of uncongenial work or because of detrimental home conditions, and it may be unfair to expect the patient to adjust under such disadvantageous conditions. Even in those cases, however, the patient should be removed only to an environment which will serve as a stimulus to the patient's recovery, nor should such segregation be regarded as a cure in itself. As a general rule, however, it is best to keep the patient in the environment in which he must live in the future, and to pursue active psychotherapy to enable him to face any environmental difficulty which may exist. Quite early in treatment the patient can be brought to see that his real difficulties lie within himself, and that he cannot run away from inner maladjustments.

The second line of inquiry grows naturally out of the history of the illness, and consists of making a survey of the patient's life. This is necessary if one finds that the current illness was a reaction to some comparatively slight strain or difficulty, and one must ask why this individual was unable to face something which would not distress the average individual unduly. The answer can generally be found in the patient's account of his life, though he himself will be quite unable to see the connection. This second line of inquiry often leads the physician to suspect that there were errors in the patient's early emotional development. If an individual is to face all the "slings and arrows of outrageous fortune," he must have a well-integrated personality, and this is only possible when the foundations of his personality have been well and truly laid. So long as life progresses smoothly and pleasantly the individual remains unaware of his fundamental weakness, nor can this be easily detected by outside observers. Only very small indications are given of this immaturity—a tendency to follow the path of least resistance, an avoidance of responsibilities, an inclination to be over-dependent on relatives and friends, or a senseless seeking after frivolous pleasure may be the only clue. Many live and die with their weakness unchallenged, others are vanquished by something which to the onlooker seems trivial. This explains why a national emergency, like the Great War

or the economic depression in America, brings to light such large numbers of mental illnesses. In more peaceful times the stress which betrays the individual's poverty of resistance may be a physical illness, the death of a relative, the loss of employment or some business worry.

Now the uncovering and rebuilding of weak foundations is by no means an easy task and generally it lies rather without the scope of the general practitioner's work. It requires great clinical skill and experience to know whether the patient is capable of discarding the props and makeshift buttresses which support his weak personality and of rebuilding his life on a sounder foundation. Such a major operation involves a period of intense dependence on the physician, who must know exactly what is happening and what to do about it. Fortunately, such a proceeding is not always necessary, as most neuroses can be resolved by less drastic means. Every psychological investigation, however, means that the patient must face facts about himself which may be unpleasant, and this may be an entirely novel experience to him. Here the physician must exercise care, for it is almost impossible for an individual to think badly of himself for very long. In the ordinary way his weaknesses and sins are quickly minimized by such mental mechanisms as *projection*, whereby the individual's own thoughts or feelings are attributed to someone else (the motorist is always ready to blame the pedestrian or the other driver for his own lack of skill or judgment), or *rationalization*, whereby we seek to justify our unconsciously determined behaviour as if it was motivated by logical thinking (the deserted wife bewails her lot unaware that her own behaviour has driven her husband away). Should unwelcome self-knowledge become too pressing, some more drastic protection must be sought, and this may take the form of a neurosis, or, in very urgent circumstances, a psychosis. Thus an individual may for years be punishing himself for some sin of which consciously he is unaware, and which he would be unable to face if it intruded itself into consciousness. The physician must therefore be careful of adding to the patient's conscious feeling of inferiority by bringing to light hidden feelings of guilt and unworthiness. Further experience will show that patients who habitually think badly of themselves are difficult to cure. It is useless to assure them that they are suffering from an unwarrantable sense of inferiority, they know that only too well themselves, but it does help them to be assured that there is a perfectly logical reason for their inferiority, and one which can with patience be uncovered and dispelled. This sympathetic, and to them rather surprising, attitude will do much to encourage them to uncover those secret sins which have haunted them probably since childhood, for even in the conscious level they feel guilty and inferior. One must not be misled into thinking that neurotics are people who live private lives of sin; the opposite, indeed, is true, because they are generally too timid, or have too rigid moral standards, to be sinful. Being shy and reserved they have often built up lurid pictures of themselves, and confession not only relieves their conscious feeling of guilt but helps to release repressed material. This was illustrated in the case of a man who, at the beginning of treatment, could remember nothing before the age of ten. After having written an account of his sex life, which incidentally was really very chaste, he began to remember incidents which occurred at as early an age as three years, and which had an important bearing upon his whole attitude to himself and to the illness from which he was suffering.



One of the first questions which the majority of patients ask is how they should deal with their phobias and obsessions. The patient is, for example, afraid to appear in company or to remain in an enclosed space; he knows that avoiding his fear only tends to make it more difficult next time, yet panic may overtake him each time he tries. The physician should make it quite clear to the patient that there is some reason for his fear and that he cannot be expected to face it unless he knows that reason. This can be illustrated by case histories or by simple analogies, such as that suggested by Yellowlees.<sup>1</sup> "If a person who is afraid of ghosts becomes aware of what appears to be a ghost standing in the doorway while he is sitting at work, he may adopt either of two methods. On the one hand, he may recall everything he has been told about ghosts, particularly that they do not really exist, and that, even if they did exist, they could not possibly hurt him. Fortified in this way, he may be brave and resolute enough to continue working at his desk, forcing himself to attend to the business in hand and to fight down the uneasy feeling that there is a strange and sinister something standing at the door. If he is of sufficiently heroic mould, he may succeed, not only in getting through his work, but in getting through it efficiently. On the other hand, he may determine to deal with the thing once for all. He lays aside his work, and by a supreme effort nerves himself to walk to the door and examine the ghost face to face. He strips it of its white sheet and mask and finds that it turns out to be, let us say, his young brother or his child just dressed up for fun, or, to put it in psychological language, the infantile in himself. If he had dealt faithfully at an earlier stage with his young brother or with his child, or with the infantile in himself, he would not have been troubled thus. Now that he has dealt faithfully with them he can return to his work, and he is no longer under the necessity of being heroic. He has no longer got to fight and conquer his fears, for the excellent reason that there are now no fears for him to conquer."

The assurance that a logical explanation for his phobia can be found will both reassure the patient that he is not just a moral weakling or "yellow," and give him hope that he will be cured. He should not, however, be allowed to think that the discovery of the hidden cause of his fear will suddenly dissipate all his fear, as certain psychologists have implied. Rather he should be told that it will give him a new attitude towards his phobia; he will feel as if he had been given an effective weapon with which to fight his adversary, now seen for the first time. His success in fighting his phobia will depend partly on his ability to face and readjust himself to the maladjustment lying behind his fear, and partly on the length of time he has been a prey to it. For habit formation plays an important, though secondary part, in the production of symptoms, and re-education is a vital part of treatment.

The patient should therefore, at the first consultation, be reassured that it is inadvisable for him to try to fight his fears without knowledge, but having discovered what he is really afraid of or why he is afraid he must then begin to make an effort. Comparatively minor or recent acquired fears should be tackled first, the patient keeping in mind all the time, repeating to himself if necessary, why he is afraid. Nor should he expect the procedure to be pleasant, for, to begin with, he will be almost as much



afraid as before. The point is that he should credit himself with a victory if he is able to do the thing he fears, whether he is afraid or not; next time he will be less afraid if he has taken the proper attitude at the first attempt, and the emotional tension will gradually lessen. Finally, he will only remember occasionally, with pride and amusement, that he is doing something of which he was formerly afraid. Each fear must be tackled and dealt with in this manner, nor should the patient be satisfied until he is able to lead a completely normal life.

Thus treatment falls into two parts, the first being one of analysis and the second one of re-education. The mistake commonly made is, of course, to miss out the first period altogether, or at least to hurry over it before the true cause has been found. It is our firm belief that no patient can deal successfully with his fears or compulsions until he can use the truth as a weapon. As Yellowlees says: "The aim of all good psychotherapy is to help the patient to face reality." During the second stage also the physician must display considerable skill in knowing just how far the patient has got in the process of re-education, and in being able to forecast what he will or will not be able to do in the immediate future, and how he will feel when doing it. This gives the patient a comforting sense that the physician thoroughly understands his case, and that he is progressing on known and expected lines. Such skill can only be acquired through clinical experience; no textbook can impart the necessary knowledge, but most pitfalls and difficulties can be avoided if the physician has an opportunity of discussing his first cases with an experienced psychotherapist.

Above all, the physician should make himself thoroughly familiar with the patient's environment. It is said that one needs to have a wide general knowledge to be a good psychotherapist, that one must be able to show some understanding of philosophies and religions, of arts and political systems, of trades, professions, and spare-time interests. This may seem a tall order, but the very nature of the work brings one in contact with people of every class, belief and occupation, and one gradually acquires information even about little-known subjects. It is, however, the patient's personal environment which the psychotherapist finds most important. He must know the people who are most important to the patient, and he must have an opportunity of forming a personal judgment of them. To-day psychiatrists think this so important that most clinics have specially trained social workers whose task it is to formulate an accurate picture of the patient's home. In particular, the attitude which the patient has to the several members of his family, and, just as important, their attitude to him and to each other, must be investigated. By this means the psychiatrist is able to estimate the stresses and strains to which the patient is continually subjected, and to direct the social worker in that manipulation of the environment which is of so much value in treatment. For example, a wife can be shown that her over-sympathetic attitude only increases her husband's fears. Thus both psychiatrist and relatives will be able to bring the same influence to bear upon the patient.

The general practitioner will have no specially trained assistant of this type, but for obvious reasons he hasn't the same need as the specialist, who only sees the patient at infrequent intervals and his family perhaps not at all. The general practitioner is often in the patient's home and, as a general rule, knows his personal environment intimately. He must make a special

point of ensuring that the patient's family understand the nature of the illness and he must outline the best attitude to adopt to the patient. Most neurotics are greatly handicapped by the crude handling, the unsympathetic attitude and lack of understanding which they suffer at the hands of their "nearest and dearest" relatives. The illness may continue unabated unless these handicaps are ameliorated. This is of the utmost importance in the treatment of nervous children, but is also vital in adult cases, as the following history shows. A man of thirty-seven suffered for some ten years from acute anxiety and many fears. The cause of his fears was analysed and treatment had progressed so favourably that he was able to do things which he hadn't been able to attempt for many years. Suddenly and without any warning his wife deserted him and his anxiety and fears returned with all their previous vigour. Now until this happened the patient had spoken little of his wife, except to remark that she was much younger than himself and that she had always been sympathetic and encouraging. Consequently it had not been considered necessary to see her, especially as the patient was poor and lived at a distance from the clinic and there was no social worker to visit the home. After he had been deserted, however, the patient confessed that he had married partly because his doctor advised it and partly because he found his own mother unsympathetic. After marriage he became intensely dependent on his wife. He used her, it seemed, as a mother substitute, for when he was afraid his one thought was to rush home and obtain her sympathy. His fears prevented him from taking her to the pictures and dances, which she craved, and even marital relations were cut down to a minimum. On these grounds her desertion was understandable, but it became more so when she confessed that she was sure he was insane and might attack her at any moment. With these thoughts in her mind her attitude towards the patient could hardly have been helpful; she was sympathetic, perhaps, but that condolence was inspired by fear rather than understanding. Nor could the patient's attitude towards her have been conducive to her happiness, marrying, as he did, to escape his mother and hoping to find in his wife the ideal mother. Cases like this illustrate the futility of attempting psychotherapy without knowledge of the patient's home life.

## THE SCOPE AND LIMITATIONS OF PSYCHOTHERAPY IN GENERAL PRACTICE

We can begin this section in no better way than by quoting T. A. Ross,<sup>1</sup> who for many years has advocated psychotherapy in general practice. "There is an idea abroad that no psychological treatment except psycho-analysis is worth talking about. I have spent my life in trying to show that this is not true. I am saying nothing against psycho-analysis, which is probably the best treatment for certain cases, but there are a great number of patients who do not need it, for whom something quite simple is all that is required. I have no wish that medical students should learn analysis. It would be impossible for them to do so even if it were desirable. Time would make it so. For the same reason, even if psycho-analysis were the only psychotherapy, mental treatment would be impossible for the majority

of patients. In my view there are, and have been for a long time, simpler and shorter methods of psychotherapy which are, at least, as old as Freud's system, and of which the greatest exponent was Dejerine of Paris. This depends on the fact that many symptoms are caused by conflicts and anxieties which are not necessarily unconscious in the Freudian sense, but which are not being faced properly." An attempt has been made in the foregoing pages to describe that "something quite simple" in treatment, and now we must try to indicate the type of patient on whom it should be practised.

In contrast to the treatment indicated for neurotic patients, analysis, even of the most mild nature, must never be practised on psychotic patients. The physician can, for his own guidance, allow the patient to pour out his troubles and, for the same reason, can make exhaustive inquiries of the relatives, but no hint of this must be given to the patient. It is, we admit, a great temptation to argue with and exhort a mildly depressed patient, but this only adds to his difficulties. Distinction must, of course, be made between a patient who is depressed and has every reason to be so because of some real trouble and the psychotically depressed patient whose degree of depression bears little or no relation to his circumstances. Treatment should be limited to physical care, guarding the patient from harming himself, and very gentle but oft-repeated reassurance and encouragement. Day after day you may tell the patient that he will, in good time, get better, that one day his depression will lift and he will then be as happy and healthy as ever he was. Meantime he must try to be patient and take what comfort he can from your reassurance. These simple platitudes may seem to have little effect, but the patient will thank you for them when he recovers. With the menopausal depression one may add that the condition is a reaction which commonly results from the physiological changes which are proceeding in the patient.

More difficulty is experienced by the general practitioner in deciding whether to undertake the treatment of a neurosis or not. One must remember that the form of treatment should be suitable to the patient's intellectual capacity and cultural status. The person of average intelligence can hardly understand analytical procedure. This may seem a sweeping statement to make, but few intelligent people have any conception of the limited power of understanding abstract theory displayed by the person of average intelligence, whose abilities are mainly confined to dealing with practical issues. The truth is that the person of average intelligence is just capable of learning to read, write and do simple arithmetic, and could not get further in education than the elementary school. Thus analysis must be limited to those who are capable of going through a high school or university education. Fortunately, those of lesser ability develop less subtle conditions than those who can understand analytical procedures. During war, officers usually suffer from anxiety or fear states, while other ranks tend to develop crude hysterias. One should therefore be guided by the rule that the less clever a patient is the more one must depend on suggestion, reassurance and simple re-education. Putting it in another way, one might say that the more intelligence a patient displays, the more passive one can become and the more one can allow the patient to analyse his own difficulties.

The non-specialist should be chary of undertaking the treatment of a long-standing condition. If the symptoms have been in evidence for more

than a few months the illness will be fixed and difficult to eradicate. If the patient has been, since childhood, a "nervous, highly strung" individual, it is probable that the current illness is but an exaggeration or exacerbation of a habitual tendency to neurotic reaction, and here, again, the non-specialist must not expect success. Another type which presents great difficulty is the patient who shows a marked reaction to comparatively trivial environmental strains, or the patient who can only produce ætiological factors which seem inadequate both to him and to the physician, because experience has shown that his real difficulties will be deeply hidden.

Age, too, is a limiting factor. After a certain age human beings become fixed in their reactions and mode of life; they resist change so much that they cannot give up defensive symptoms, no matter how inadequate these are. Individuals differ widely, of course, in this respect, but on the whole, patients above the age of fifty are not suitable subjects for psychotherapy. Fortunately it is uncommon to find a neurosis developing so late in life, though an old neurosis may persist to a much later age. When middle age is passed the individual usually reacts to difficulties by developing a psychosis rather than a neurosis.

Of the different neuroses themselves the physician will find greatest success in treating the simple hysterias and the mild anxieties and phobias. Generally speaking, he should avoid obsessional states, for even specialists are chary of undertaking treatment of these cases, despite the fact that they are often eager to be psycho-analysed.

A final limitation applies to the physician himself and is one which he may find difficult to judge. It should be obvious that one cannot expect to obtain results in psychotherapy unless one has a special aptitude for it, just as one cannot paint a picture or play a sonata unless one is gifted in a special way. Psychotherapy, whatever its too ardent supporters may say, is more of an art than a science, and for its practice one must have, in addition to training and knowledge, an intuitive, inborn capacity. Unfortunately some physicians, who are particularly obtuse about themselves, think that they have this gift and consequently practise what they imagine to be psychological treatment with meagre results. Any success that they do have depends on the powerful suggestive quality of their own belief in their skill. The physician may judge his capacity to practise this difficult art by the degree of his interest in it, by his liking for it, by his capacity to understand how neurotic patients think and feel, and, of course, by the results he obtains, though this last is hardly a criterion for the beginner.

It may be thought that we have imposed so many limitations that the physician will have difficulty in finding suitable cases to treat. This is far from the truth; in every community there are large numbers of unhappy people who are suffering from some degree of psychological maladjustment. They do not come to the physician complaining that they are neurotic, but that they cannot sleep, or are run-down or have vague pains or strange feelings. Indeed, the general practitioner will find the patient who complains of physical symptoms the most easy to help. Let him keep in mind that emotional disturbance has a physical concomitant in everyone. The patient with a chest will perhaps have asthma, the patient with a tendency to gastric disorder will produce symptoms of ulceration in that region in response to some emotional or mental crises. Others who have no such bodily safety-valve will perhaps produce a more easily recognized neurosis.

It behoves every physician to keep this possible ætiology in mind, and if he does so he will not lack material.

In conclusion, the reader may have found less concrete directions for the treatment of psychological conditions in this chapter than he expected. He must remember that this subject is one which can be learned best by practice, and that most attempts to teach or write about it have, as Lewis says, "no reality until given body and meaning in the individual case." He may have found the explanations given here unnecessarily complicated, but must reflect that human nature is unbelievably complex and that simple interpretations are rarely correct. Like most writings on this subject, this chapter may give the impression of irritating vagueness; in this case the lack of sufficient space is partly responsible, but also it must be remembered that there are large gaps in our knowledge which psychologists are constantly trying to fill.

## ALCOHOLISM AND DRUG ADDICTION

### ALCOHOLISM

Though accurate statistics do not exist, there is undoubtedly less hard drinking in this country to-day than there was, say, at the beginning of this century. Drunken men and women are seldom seen in the streets, Saturday night is no longer the time of carousal it used to be and convictions for drunkenness have decreased. These changes are partly due to the enormous increase in the price of liquor and partly to a change in social and moral codes. None the less, the abuse of alcohol by a certain proportion of the population still constitutes a grave social problem and causes untold suffering to the individual and his relatives. Because of the general decrease in the abuse of alcohol there is much more moral stigma attached to addiction and the addict is more inclined to drink in secret. Doctors, on the other hand, are becoming more conscious that alcoholism is a medical rather than a moral problem. In America the issue is more acute, for with prohibition came a wave of alcoholic excess which beggars description. Hospital wards, psychopathic hospitals and institutions for mental disorders were, and to a lesser extent still are, filled with alcoholic illness of all degrees and varieties. This has led to an intense study of these conditions and to the more recent advances in ætiological and therapeutic knowledge.

Mention should first be made of the part which avitaminosis plays in alcoholic disorders in general. According to recent research alcohol does not have a direct toxic effect on the nerve tissue in alcoholic polyneuritis (see p. 399) and Wernicke's disease, but the clinical manifestations arise rather from avitaminosis inaugurated by the chronic ingestion of alcohol. According to Alexander (1939)<sup>1</sup> there is much suggestive evidence that Korsakow's psychosis and delirium tremens may also be due essentially to vitamin deficiency. Brodsky (1938)<sup>2</sup> reports that injections of massive doses of crystalline vitamin B (5 to 10 mg. daily) are followed by prompt improvement and complete disappearance of symptoms in cases of chronic alcoholic psychoses. Mainser and Krause (1939)<sup>3</sup> report good results from the treatment of delirium tremens by nicotinic acid. Much of the work on

vitamin deficiency in chronic alcoholism is new, but promises to be a field rich in therapeutic results. The deficiency is due to three main factors:—

- (a) Chronic alcoholics of all classes are notoriously neglectful of their diet.
- (b) Gastritis and defective liver metabolism cause incomplete absorption and storage of vitamins and minerals.
- (c) Alcohol has a high calorific value, which necessitates an increased supply of vitamins, especially B. Alexander therefore concludes that in order to secure optimum therapeutic results it is best to give very large amounts of vitamins A, B<sub>1</sub>, B<sub>2</sub> and C in all types of chronic alcoholic disease.

The excessive use of alcohol gives rise to a variety of disorders, which are classified as *acute* or *chronic*. Here we are concerned with the therapeutic aspect, and for the sake of clarity and simplicity we shall consider the disorder “acute” when the patient may be a danger to himself or others.

**Acute Alcoholism.**—*Acute or subacute alcoholic poisoning* results from drinking large amounts of alcohol in one or several bouts. Accurate diagnosis is important not only because of treatment but because death from acute or subacute alcoholism must be reported as a case of poisoning. Ideally, specimens of blood (at least 10 c.c.) and urine should be obtained for toxicological analysis. *Dipsomania* is a state of periodic acute intoxication and is usually regarded as being symptomatic of an underlying manic-depressive psychosis of epilepsy. *Mania à potu* occurs in individuals who are susceptible to alcohol and who become intensely excited and perhaps dangerous after taking comparatively small amounts.

Treatment of these conditions should be directed to detoxication and to obtaining rest. The stomach should be washed out through a soft stomach tube with warm water. Colon lavage with normal saline and, later, saline purgatives also reduce auto-intoxication. Apomorphine hydrochloride,  $\frac{1}{16}$  gr. (6.5 mg.) subcutaneously, is strongly recommended<sup>1</sup> for its twofold action of clearing out the stomach and giving restful sleep. Other sedatives are barbitone x gr. (0.6 gm.), paraldehyde, at least 3 drachms (10.8 c.c.) by mouth, or morphia  $\frac{1}{4}$  gr. (16 mg.) and hyoscine  $\frac{1}{16}$  gr. (0.6 mg.) hypodermically. It should be noted that paraldehyde rarely, and hyoscine more commonly, may cause delirium rather than rest.

**Delirium Tremens or Acute Alcoholic Delirium.**—In this condition it is important to recognize the earliest manifestations, since prompt treatment may avoid the more serious sequelæ. Delirium tremens occurs usually during an excessive bout of drinking when rest and diet have been scanty. Hours or even days before the onset of the psychotic symptoms certain clinical manifestations make their appearance. Tremors, motor restlessness, flightiness of thought and apprehensiveness are danger signals. Other prodromal symptoms are nausea, profuse sweating, headache, rapid pulse and fever. The patient is either sleepless or, if he does sleep, is wakened quickly by nightmares. If treatment is not instituted at this stage the typical delirium appears rapidly with hallucinations and disorientation.

A therapeutic régime somewhat as follows should therefore be adopted:—

- (a) Alcohol should be stopped immediately and thereafter avoided entirely. To begin with this presents little difficulty, for owing to

the confusion of the patient there is little demand for it. If there are symptoms of collapse, 1 to 2 c.c. of nikethamide should be given intramuscularly every four hours for six doses.

- (b) For sedative treatment 3 to 4 drachms (10·8 c.c. to 14·4 c.c.) of paraldehyde once to thrice daily are recommended. A too liberal use of sedatives should, however, be avoided, and in preference frequent warm baths should be given. The use of mechanical appliances to restrain the patient forcibly is contraindicated, though this may require an increased nursing staff. If the patient is sleeping he should not be wakened on any account.
- (c) For elimination 1 oz. (31·1 gm.) of magnesium sulphate should be given, and this may be repeated each morning unless there have been four evacuations on the previous day. Two grammes of sodium chloride should be given in capsules four-hourly in order to encourage the retention of fluids in the tissues (Bowman and Keiser).<sup>1</sup> Although the studies of Cline and Coleman (1936)<sup>2</sup> and Piker and Cohn (1937)<sup>3</sup> suggest that fluids should be limited and spinal puncture performed to relieve oedema of the brain, yet later work by Bowman and Keiser (1939)<sup>1</sup> indicates that the reverse type of treatment with salts and forced fluids to relieve systemic acidosis and dehydration is preferable.
- (d) The diet should be soft or liquid and of a high vitamin content. Daily intramuscular injections of from 5 to 10 mg. of vitamin B<sub>1</sub> (see p. 400) and nicotinic acid, 0·5 gm. by mouth, in divided doses have been recommended.
- (e) Psychological analysis of the factors underlying the alcoholism should be carried out after the acute phase has passed.

As can be seen, there may be difficulty in carrying out the above régime in the patient's house. Sometimes, however, there are no suitable hospitals available and the family doctor has perforce to treat the patient at home. In such cases trained nurses should be engaged and relatives discouraged from taking any part in the routine.

*Alcoholic Psychoses.*—Psychotic reactions to alcohol require little discussion in this volume, for they necessitate treatment under certificates in a mental hospital. *Alcoholic confusion* is a rare condition which results from sudden and heavy drinking; it is a state allied to other toxic confusional psychoses. The patient is excited, restless, confused in thought and action and may be hallucinated and have fear reactions. There is not much physical upset. Depression and remorse set in with recovery. *Acute alcoholic hallucinosis* is not uncommon and often accompanies delirium tremens. When threatening auditory hallucinations and delusions of persecution without disorientation occur, hospitalization should be carried out immediately, for such patients are suicidal and unmanageable. Rarer conditions are delusions of jealousy and paranoid reactions. *Korsakow's psychosis* is a serious condition in which there are few satisfactory recoveries. The patient should always be sent to a mental hospital and relatives warned that several months' observation will be required to determine whether

this will have to be a permanent arrangement. The earliest symptoms are defects of memory, dizziness, headache and mild confusion. It is usually accompanied by signs of neuritis. Rosenbaum and Mcrritt (1939)<sup>1</sup> have made a valuable study of the factors important in prognosis.

**Chronic Alcoholism.**—When a patient harms himself or his family by drinking to excess and cannot be made to realize it, or when he no longer has the will or strength to overcome his habit, he should then be regarded as suffering from chronic alcoholism (Diethelm).<sup>2</sup> The development of somatic and personality changes and not the frequency of the bouts of intoxication are the features on which the diagnosis should be based. The only treatment which is flexible enough to be applied to all cases is a combination of personality analysis and re-education under strict supervision.

Ideally every case of chronic alcoholism should be treated in a special institution or hospital where continuous supervision can be given and where there are facilities not only for psychological and medicinal treatment but also for work, games and discipline, which form such an important background to a successful cure. Special institutions for the treatment of alcoholism are a rarity in this country; there are none, for example, in Scotland. They are also comparatively expensive and only a small percentage of patients can afford the fees. There are, however, a number of private hospitals and nursing homes which specialize in the treatment of nervous and mental disorders which are suitable for the treatment of alcoholism. In the writer's opinion too little use is made of the admission blocks of mental hospitals for patients who are unable to afford large fees or who are in the rate-aided classes. By persistent and skilful persuasion many addicts who bring misery to themselves and their families could be induced to become voluntary patients in mental hospitals. But even if full use were made of the existing institutions and hospitals the family physician would find that he was compelled to treat a certain number of patients in their own homes. This presents the greatest difficulty and should only be undertaken in the last resort, for adequate control is uncertain even where nurses are in attendance.

The second major difficulty is to decide whether alcohol should be withdrawn abruptly or "tapered off." The writer has no doubt that abrupt withdrawal is physiologically and psychologically correct in all cases, and this belief is supported without exception by all the recent publications of American authorities who have had a very wide experience in the treatment of alcoholism. Alcohol differs from other drugs like morphia and cocaine in its physiological effects, for the patient does not develop the same physiological need, or the same tolerance, nor does sudden withdrawal lead to the serious symptoms which occur with other drugs. Diethelm<sup>3</sup> states: "There are no serious symptoms of withdrawal and no danger of the development of delirium tremens. Although the average physician claims that he has seen delirium tremens caused by abrupt withdrawal, there are no carefully studied cases in the literature to substantiate this claim." Abrupt withdrawal is also important psychologically, for it shows the patient that there is no medical necessity for alcohol in his case, the realization of which is the beginning of his re-education. In this country there is considerable



support given to the theory that abrupt withdrawal *may* be followed by an acute mental state in the nature of a delirium, and it is said that restlessness, excitement and irritability may be so great that unless one deals with the patient sympathetically by allowing some alcohol one loses all contact with him at once. It is true that sympathetic handling must be the keynote of the treatment of alcoholics, but the writer doubts whether the patient will later respect and trust the physician who gives in to his importunities as much as he will the physician who firmly guides him over the first difficult days. The detoxication period is, after all, the shortest and by far the easiest part of the treatment. In the writer's opinion, exception should only be made under two circumstances: first, when the patient is old and feeble and has had a long history of alcoholism; and, secondly, where the patient is being treated in his own home where nursing and other facilities are inadequate. Information regarding the advisability or otherwise of abrupt withdrawal in the latter category is still largely a matter of hearsay, and general practitioners should take every opportunity of carrying out abrupt withdrawal in an attempt to throw some light on what can and what cannot be done. When "tapering" is practised the patient's consumption should be reduced by 25 per cent. each day, so that the whole process takes less than a week. Paraldehyde can be added to the alcohol, for its penetrating odour and taste prevent the patient from knowing how much alcohol he is having, as well as for having a sedative effect.

When possible, then, the patient should spend at least the first two months of treatment in a hospital where absolute supervision and skilled psychotherapy can be given. When the patient is treated at home the first stage should begin where possible with the immediate and absolute withdrawal of alcohol. The patient should be told that he has no need to fear withdrawal symptoms, and certainly not delirium tremens. If required, the use of stimulants, such as nikethamide, is permissible. Bloomberg (1938),<sup>1</sup> Reifenstein and Davidoff (1930)<sup>2</sup> advocate the use of amphetamine, in doses of 10 to 30 mg. daily, to relieve depression and to produce a latent interval of sobriety during which psychotherapy may be inaugurated. The patient is usually co-operative for the first month and then begins to be resentful of restraint and unwilling to continue treatment on the grounds that he is completely cured. Unhappily he is often supported in this by his relatives, either because of expense or because they are deceived by the patient's improvement and optimism. The second phase of treatment, which consists of a reorientation of the patient's habits and outlook on life, is, however, most important. Many patients supposed to be cured are still left a prey to the very factors which were originally responsible for their addiction to alcohol. Too little attention is paid to personality analysis and adjustment by skilled psychotherapy, but there is a growing number of special departments attached to general hospitals where adequate domiciliary treatment is available.

The patient should be at work, but his spare time should be well occupied with social activities and physical exercise. Once or twice a week he should see his physician to discuss current difficulties and the management of his life. He must gradually develop fresh interests and group activities and reacquire confidence in his ability to face disappointments, failures or

depressions without the help of alcohol. When cured he should have a positive feeling that he has no need of alcohol. Nothing less than total abstinence should be the object in view and all pleas for moderate drinking should be disallowed.

It is important to carry the co-operation of the relatives throughout the various stages of treatment. They should understand that old associations must be broken, that they must be as abstemious as the patient is trying to be and that they must endeavour to make life new and interesting to him. Relatives are often unable to understand that alcoholism is an illness, preferring to regard it as a moral weakness. Though the majority do their best under exceptionally difficult circumstances, some wives seem to find a perverted satisfaction in sacrificing themselves and their children and are unwilling to co-operate with the physician in enforcing treatment; others, discouraged by broken promises and constant relapses, become indifferent and give the patient no help.

Full discussion of the psychobiological factors underlying alcoholism must be left to works on psychopathology, but some of the commonest can be mentioned briefly. Aetiological factors are seldom on a conscious level and this accounts for the inadequacy of conscious motives and wishes in correcting the desire for alcohol. Smalldon (1933)<sup>1</sup> believes that the underlying psychological factor is best explained on the Freudian hypotheses (*e.g.*, latent homosexuality, repressed sexual forces, partial oral fixations and sadism supply the driving force of desire for alcohol), and that this theory is more acceptable than any other. Knight (1937)<sup>2</sup> calls attention to the fact that the mother of a male patient is usually over-indulgent and protective, quick to satisfy his infantile distresses, vacillating in training and fostering the desire to take something into his mouth for comfort and relief. Such early training stimulates an excessive desire for personal affection which, in later life, is doomed to frustration. Alcohol is used as a solace for the depressing emotions caused by the contrast between early pampering and the frustrations of the adult world. Solitary drinkers are often lonely persons who drink in order to forget their longing for normal social life. Shy, sensitive people seek enough confidence to greet their fellows. An anxiety neurosis or a depression may be the causative factor; nor must we forget that suggestible, inadequate personalities, whether or not complicated by low intelligence, are easily persuaded to form drinking habits. There are trades and occupations which encourage alcoholism, and even big business does not despise the aid of alcohol in dealing with customers. Certain games and sports have Bacchus as their patron and the devotees must worship the same god. Considerable controversy exists as to whether people drink primarily for the immediate sensory pleasure of taste; authorities who themselves are abstainers deny this in a somewhat intolerant manner, but it is generally admitted that taste does not play a major part in the formation of drinking habits.

### DRUG ADDICTION

The treatment of drug addiction is based on the same principles as described above for alcoholism, for both conditions point to a personality disorder from which the patient must be freed after the toxic influence of

the drug is relieved. There is this difference, however, that in drug addiction the psychological changes following prolonged use are more profound, the symptoms due to withdrawal of the drug more grave and the craving more intense. The development of tolerance is also important, for the addict takes more and more of the drug to satisfy his cravings. His tolerance to the drug still further increases and a vicious circle develops. The general physical deterioration is also greater in drug addicts than in alcoholics.

**Morphine Addiction** is the most common form of drug habit in this country, the largest group being formed by those who can obtain supplies easily; thus the highest incidence occurs in doctors, nurses, chemists and their relatives. The craving may have been formed after a long illness in which morphia has been given for the relief of pain. Patients have been known to malingering in order to have another operation and more morphia; the writer has seen an addict with the scars of thirty-six abdominal operations. It therefore behoves doctors, and especially surgeons, to regard every patient as a potential morphia addict and to exercise corresponding care in prescribing.

Treatment should always be carried out in a hospital where psychological care can be given and where the patient is under discipline. Statutory provisions are of little help, and, in our opinion, a special type of certification should be available. Attempts to treat addiction without restriction ignore the extent of the physiological craving and the complete inability of the patient to co-operate honestly. It is permissible to give morphia to the patient while arrangements are being made for hospitalization, but once this has been accomplished abrupt withdrawal of the drug should take place. The dreaded symptoms of withdrawal have been much exaggerated, and with good medical care and intensive psychotherapy they can be greatly modified and controlled. Subsequent treatment consists of psychotherapy and re-education on the lines suggested for the treatment of chronic alcoholism (see p. 916).

**Cocaine Addiction.**—This is fortunately uncommon in this country. It is found especially among criminal and depraved classes. Unhappily every addict is a potential source of danger to the community. The sexual and other urges which follow indulgence make him crave for company and induce him to pervert others. Tolerance, it is important to note, is not acquired, and the increase in consumption is due mainly to a craving for increased sensations. There are no physical symptoms attributable to withdrawal of the drug. Cocaine should, therefore, never be given to a patient who comes for help, no matter what hysterical symptoms he may show or what threats he may make. Treatment should be undertaken in hospital, the drug should be stopped at once and sedative and eliminative treatment instituted. Psychotherapy and re-education play a fundamental part in the management of the case.

D. R. MACCALMAN.

# TECHNICAL PROCEDURES AND OXYGEN THERAPY

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## TECHNICAL PROCEDURES

**T**HE procedures to be described in this chapter must be carried out in an aseptic manner. The techniques of hospital or nursing home may have to be modified in general practice, and it will be convenient to begin with an account of the steps common to all.

*The hands and forearms of the operator* are cleansed by washing for five minutes, preferably in running warm water. A bottle of spirit soap may be carried for this purpose. The use of the nail-brush should be confined to the nails and nail-folds; elsewhere it leads to roughening of the skin. The washing should be done from the elbows downwards, and the final rinsing is of the hands alone. The hands are then dried on a sterile towel. If this cleansing is, as it should be, scrupulous, it is unnecessary to wear gloves. *The skin of the patient* should be shaved if the part is hairy. Antiseptic solution, e.g., 5 per cent. Liquor Antisepticus, must not be "slopped" over the area, lest it reach and irritate distant parts—for example, the genitalia, in preparing the abdomen. To *drape the sterilized area*, it is convenient and economical to employ towels 2 ft. square, with a hole 2 in. square in their middle; a number of these, and a supply of gauze mops, may be sterilized in a drum (in hospital or nursing home, or by a commercial firm), and used as required. The quantity of *local anæsthetic* needed for these minor procedures is best purchased in ampoules; the exterior of these, and the file for opening them, are sterilized by immersion in a mixture of lysol (1 part) and spirit (3 parts) for five minutes.

**Sterilization of Syringes and Needles.**—The importance of adequate sterilization of syringes both in domiciliary and hospital practice deserves emphasis for several reasons. Injections are being used with increasing frequency in medical practice; the traditional methods of sterilizing syringes, as by immersion in spirit, are more seriously inadequate than is generally appreciated; and recent work has shown that the danger of transference of infectious hepatitis must be added to the better-known danger of local organismal infection. A detailed account of the problems involved and techniques recommended will be found in the M.R.C. War Memorandum No. 15 on "The Sterilization, Use and Care of Syringes."

The following facts should be noted:—

Spirit does not kill sporing organisms and cannot be trusted to sterilize a glass-metal syringe contaminated by non-sporing pyogenic organisms.

Boiling in water will destroy all pathogenic organisms except those bacteria producing resistant spores.

Only sterilization by autoclave or hot-air oven (160° C. for not less than one hour) can be trusted to destroy all organisms, but glass-metal syringes cannot be treated in this way.

A syringe or needle, though adequately sterilized, may be contaminated with pyogenic organisms during assembly and use by contact with fingers, non-sterile fluids, dust or air-borne droplets, or by contact of the needle with a non-sterile surface.

Routine intravenous injections involve the danger of transference of the infection, probably due to a virus, which results in jaundice from 40 to 160 days later. This condition has been called "delayed post-arsphenamine jaundice," "yellow fever vaccine jaundice," "homologous serum jaundice," "syringe hepatitis" and other names. It has been demonstrated that the transference of 0.1 c.c. of infected serum is enough to cause the disease, and several reports show an incidence of over 50 per cent. after mass intravenous injections by the traditional routine.

All who use syringes for injection or aspiration should therefore take the following precautions :—

It is essential to keep syringes for injection separate from those used for aspiration.

Whenever possible, all-glass syringes should be used and they should be sterilized with needles by autoclave or hot-air oven.

When glass-metal syringes must be used, or if an autoclave or hot-air oven is not available, "sterilization" by boiling is the method of choice.

*Sterilization by Boiling.*—A layer of lint is laid in the sterilizer and the component parts of the syringe with the needle and two pairs of forceps are placed on it. The needle should be threaded on a separate piece of lint. Cold or warm water is added and is brought to the boil and kept boiling for not less than five minutes. Tap water can be used unless it is hard, when rain water or distilled water is preferable.

After boiling, the syringe must be allowed to cool with minimum exposure to the air. If a sterilizer is used, the tray should be lifted out and placed on the inverted lid while the water is emptied from the sterilizer: the tray and lid are then replaced and left to cool. If the syringe and needle have been boiled in an improvised sterilizer such as a saucepan, a lid should be obtained, kept on the saucepan during boiling and replaced after as much as possible of the water has been poured off to let the instruments cool.

When the syringe is cool it should be removed by forceps sterilized by boiling (or alternatively by flaming). The assembly of the syringe can safely be done with dry washed hands if the syringe itself is dry and there is no risk of water which has touched the fingers running over other parts of the syringe or needle. If this is done, care must be taken to touch only the outside of the syringe and the handle of the piston.

The needle should be fixed to the barrel by means of the sterile forceps and not touched with the fingers. The assembled syringe is then returned to the empty sterilizer and covered with the lid until it is used.

*Disinfection by Chemicals.*—The only chemical disinfectant which is suitable for use with syringes is diluted alcohol. Other chemicals are less reliable

and more likely to destroy the material to be injected. The use of alcohol is justifiable only when the syringe is to be used exclusively for injections (other than intravenous) of sterile fluids such as insulin, and when sterilization by heat is impracticable. When it is to be used, all-glass syringes should be employed. The alcohol should be diluted to a strength of 70 to 75 per cent. by volume with sterile (boiled) water. Four parts of industrial methylated spirits with one part of water give the required strength.

After thorough washing in clean tap water the syringe should be assembled and the spirit sucked up and down two or three times *through the needle*. The parts are then dismantled and completely immersed in the spirit in a covered vessel for at least five minutes. Forceps which have been half immersed in spirit for a similar period or sterilized in a flame should be used to remove the syringe from the spirit and to attach the needle. If the spirit is to be washed out of the syringe, water which has been freshly boiled and allowed to cool in the same container may be used, but autoclaved saline or distilled water are better.

*Mass Injections.*—Particular danger of cross infection arises in conducting mass inoculations or mass intravenous injections such as are required in a V.D. clinic. In all such circumstances safe practice depends on the efficient organization of the routine to be practised by a team which should consist of at least four persons—the doctor who gives the injections and three assistants. One assistant assembles and fills the clean syringes, a second cleans the used syringes and needles and a third marshals the patients and keeps the records. Whenever possible, the syringes should be of the all-glass type and sterilized by autoclave or hot-air oven.

When inoculations are hypodermic or intramuscular, it is sufficient to use a newly sterilized needle for each patient.

When injections are intravenous, it is essential to use a freshly sterilized syringe as well as needle for each patient to avoid the transference of the minute quantity of serum which is sufficient to cause syringe hepatitis. If the supply of syringes is insufficient to permit resterilization by autoclave or hot air, or if the syringes are of the glass-metal type, each syringe and needle should be flushed out after use with a cold 2 per cent. solution of lysol, washed in warm soapy water, rinsed with water, boiled and finally rinsed in a fresh bottle of sterile saline.

### SUBCUTANEOUS ADMINISTRATION OF FLUID

Normal saline (0.9 per cent.) is readily absorbed from subcutaneous areas rich in lymphatic vessels. A "drip" apparatus is used, the delivery tube of which leads to a Y-tube, from which two rubber tubes conduct the fluid to two special "subcutaneous saline" needles. These are of medium bore, and have additional lateral apertures. All the component parts must be sterile. A "head" of about 2 ft. is usual. The system is filled with saline solution, and the delivery tube clamped. The needles are inserted through intradermal wheals of local anæsthetic solution. They may be placed (1) at the outer border of each pectoralis major muscle, directed towards the apex of the axilla; or (2) on the antero-internal aspect of each thigh, near and directed towards Poupert's ligament. Care must be taken that they do not puncture or rest in a blood vessel. When they are correctly placed the

delivery tubes are connected to them by adaptors; the needles and adaptors are then covered by a piece of sterile gauze, and fixed in position by strapping. The "dripper" is adjusted to deliver 40 to 50 drops a minute. If 10 c.c. of 2 per cent. novocain solution is added to each litre of saline solution, the method does not give rise to pain. The axillæ (or groins) are inspected from time to time, and if the tissues appear tense, or unduly œdematous, the flow is temporarily stopped. By giving one and a half litres of saline each day by this route, sufficient sodium chloride for metabolic needs is supplied. Occasionally the apertures in a needle become blocked, but this is easily remedied by "stripping" the corresponding delivery tube towards the needle.

### RECTAL ADMINISTRATION OF FLUID

Before fluids are administered by the rectum it should be thoroughly emptied by an enema. By this route may be given: (1) tap water, which is very well tolerated; (2) normal (0.9 per cent.) saline solution; (3) normal (5 per cent.) glucose solution; and (4) a mixture of (2) and (3). The successful use of the method depends on the avoidance of any distension of the rectum, as this leads to expulsion of its contents.

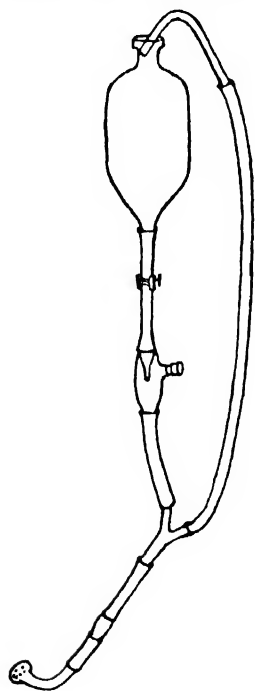


FIG. 24.—Apparatus for Rectal Administration of Fluid.

The apparatus, which need not be sterilized, consists of (1) a "drip" apparatus, which is connected by (2) thick-walled rubber tubing to (3) a wide-bore rectal nozzle of glass or, better, vulcanite (the nozzle used by radiologists for the introduction of a barium enema is a good pattern), and (4) a Y-tube with an additional length of rubber tubing, connected to (5) a glass J-tube. The apparatus is arranged as shown in Fig. 24. The purpose of the thick-walled tubing is to prevent kinking, in order that if necessary flatus may escape by the free limb of the Y-tube, which is hung on the container by the glass J-tube. If the anus is sensitive, a little anæsthetic ointment<sup>1</sup> may be smeared on the nozzle. The tubing near the nozzle should be loosely secured to the thigh by a turn of a bandage, rather than by adhesive strapping; the removal of the latter from such a hairy part is painful. A "head" of about 12 in. is all that is necessary, and a suitable rate of flow is 40 drops per minute, or 150 c.c. per hour. The flow may be stopped for one hour in every four, but the

nozzle is left in position, unless the bowels are to be moved. Thus about 2.5 litres of fluid may be given in each twenty-four hours. An alternative method is to run into the rectum through a catheter (size 12) attached to a funnel 300 c.c. of the desired fluid every four hours. The rectum must be washed out daily.

Occasionally hypertonic solutions are administered by rectum, in order to procure a fluid evacuation and thus to favour the reduction of intracranial

<sup>1</sup> Such as Benzocaine.

pressure. For an adult, 4 to 6 oz. (120-180 c.c.) of a 50 per cent. solution of magnesium sulphate are given slowly by catheter and funnel; the enema must be retained for twenty to thirty minutes to allow time for its hydropic action.

### VENIPUNCTURE

Puncture of a vein may be necessary (1) for the intravenous introduction of fluid or drugs or (2) for the withdrawal of blood, to obtain a sample for analysis, to obtain blood for transfusion, or to deplete the circulation as a therapeutic measure. For any of these purposes, as a rule, a vein in one of the antecubital fossæ is chosen; but sometimes (*e.g.*, in obese patients) the long saphenous vein is more accessible. Veins may be visible and prominent, and then they have an irritating habit of slipping easily from side to side under the skin, as if they were actively eluding the point of the needle. When this difficulty is extreme, it may be overcome by transfixing the vein from side to side with the finest hypodermic or cambric needle available, so that it is immobilized; the vein is then punctured distal to the immobilizing needle. In an obese arm the antecubital veins may not be visible, but as a rule they are palpable when engorged. In practice the least movable vein which can be identified should be utilized. Before a vein is punctured it should be made as prominent as possible; several manoeuvres are available:—

- (a) A tourniquet may be applied at the root of the limb, so as to obstruct the venous return without stopping the arterial inflow. This may be a turn of bandage twisted on itself; a piece of rubber tubing applied over a towel and fastened by a forceps, or the cuff of a sphygmomanometer inflated to a pressure of about 80 mm. of mercury.
- (b) The limb may be allowed to hang over the edge of the bed for a few minutes before the puncture.
- (c) The distal part of the limb, up to the site of puncture, may be heated by a hot fomentation, or by immersing it for ten minutes in hot (120° F.) water.
- (d) (Arm.) After the application of the tourniquet the patient may be directed to grasp a roller bandage firmly with his hand at intervals of thirty seconds.

In difficult cases a warm antiseptic solution, 5 per cent. Liquor Antisepticus, should be used for cleansing the skin; the cooling action of spirit or ether causes the veins to contract.

**Intravenous Medication.**—A fine hypodermic needle should be employed. The fluid to be injected is taken up out of its container, through the needle, into a syringe of appropriate size. The needle should not be passed to the bottom of, *e.g.*, an ampoule, as its point may be turned by this fault; but the ampoule should be tilted to allow all the fluid to be drawn up with the needle resting on the wall. The syringe and needle are then held vertically, needle uppermost, the barrel is tapped to dislodge any bubbles of air, and the piston pushed onwards until fluid flows from the point of the needle. The needle is pushed through the skin a little to one side of the selected vein, and then brought over it, ready to make the puncture. When the



vein is large, the position of the bevel of the point does not matter, but when the vein is small the bevel should be held downwards, as this minimizes leakage. The needle is then pushed into the vein at an acute angle, and its position verified by slowly<sup>1</sup> withdrawing a little blood into the syringe. When the point is correctly placed, the obstructing cuff or tourniquet is removed and the contents of the syringe slowly injected. *An injection should never be made unless blood has been withdrawn into the syringe, and after this has been done the position of the needle should not be altered until the injection has been completed.* The needle is then quickly withdrawn while the thumb of the left hand makes pressure upon the area of the puncture through a gauze swab or piece of sterile cotton-wool; if the patient flexes his elbow on this pad for a few minutes a dressing is not required.

If the patient moves there is a possibility that the needle may have been dislodged from the vein, and its position within the vein must be verified afresh before the injection is begun or completed. During the injection, if any swelling appears under the skin round the puncture, leakage has occurred, and the injection should be stopped at once, the needle withdrawn, and a new vein in another limb utilized. A hot fomentation, renewed four-hourly over the area of leakage, is the best method of minimizing local irritation.

**To Obtain a Sample for Analysis.**—If possible, samples of blood for analysis should be taken from the patient at least eight hours after his last meal (*e.g.*, in the morning before the patient's breakfast); if this is not possible, the interval after the previous meal should be indicated to the laboratory. Samples should be transmitted to the laboratory as soon as possible after their withdrawal. For a single estimation 5 c.c. suffice; for several different estimations 10 to 15 c.c. are necessary. The nature of the samples required for the quantitative estimation of certain constituents of blood, and the normal range of these, are indicated in Tables I and II. When untreated blood is required it is withdrawn into a syringe by venipuncture and transferred to a sterile test-tube fitted with a *rubber stopper*. When an oxalated sample is necessary, blood withdrawn into a syringe is transferred to a similar test-tube containing a small knife point of crystals of potassium oxalate as an anticoagulant, the test-tube being shaken to ensure solution of the crystals. In practice, it is often very convenient to employ "Venules"<sup>2</sup> for the collection and transmission of samples of blood. These are small vacuum tubes fitted with a sterile hollow needle; they may be obtained with or without the addition of, *e.g.*, potassium oxalate crystals.

**To Obtain Blood for Transfusion.**—See p. 939.

**To Deplete the Circulation.**—Venipuncture has replaced venesection as a method of depleting the circulation; in general, the indications for the procedure are cardiac failure, with backward pressure in the systemic veins, hypertension, uræmia and polycythæmia. The technique is similar to that employed in the withdrawal of blood for transfusion: up to 500 c.c. of blood may be withdrawn; often it must be discarded, but it is a good plan to group such patients, for the blood may occasionally be utilized for transfusion, if direct matching (p. 936) shows it to be completely suitable, or it may be possible to store its plasma for future use.

<sup>1</sup> Strong suction may draw the wall of the vein over a correctly placed needle, and so prevent the withdrawal of blood.

<sup>2</sup> "Venules," Messrs Behring.

TABLE I

BIOCHEMICAL ESTIMATIONS, TESTS, ETC., FOR WHICH UNTREATED BLOOD IS REQUIRED

Constituent.	Normal Range.
Inorganic Phosphate . . . . .	3.0-4.5 mg. per cent.
Calcium . . . . .	9-11 " "
Sodium . . . . .	315-340 " "
Potassium . . . . .	16-22 " "
Bilirubin . . . . .	0.1-0.5 " "
Icteric Index . . . . .	4-6 units.
Acid Phosphatase . . . . .	4-6 " "
Alkaline Phosphatase . . . . .	6-12 " (King) (King)

Van den Bergh's reaction.

Widal and other agglutination reactions.

Wassermann reaction. Kahn reaction.

Serum for grouping or direct testing before transfusions.

Whole blood for culture, transferred direct to flask of medium.

TABLE II

BIOCHEMICAL ESTIMATIONS AND TESTS FOR WHICH OXALATED BLOOD IS REQUIRED

Constituent.	Normal Range.
Sugar . . . . .	80-120 mg. per cent.
Urea Nitrogen . . . . .	10-15 " "
Non-protein Nitrogen . . . . .	25-35 " "
Creatinine . . . . .	1-2 " "
Uric Acid . . . . .	2-4 " "
Cholesterol . . . . .	140-200 " "
Chlorides (as NaCl) in Whole Blood . . . . .	450-500 " "
Chlorides (as NaCl) in Plasma . . . . .	570-620 " "
Alkali Reserve. (CO <sub>2</sub> Combining Power) . . . . .	55-75 vols.
Total Plasma Proteins . . . . .	6.0-8.5 gm. per cent.
Albumin. (Plasma) . . . . .	3.6-5.6 " "
Globulin. (Plasma) . . . . .	1.3-2.5 " "
Fibrinogen. (Plasma) . . . . .	0.3-0.4 " "

Red blood corpuscles, for grouping or direct testing before transfusions.

## INTRAVENOUS INFUSION

Fluid may be introduced into a vein either through a needle or through a cannula; for the latter procedure the vein must be exposed. The chosen fluid may be given in one dose, by allowing it to flow continuously, or its administration may be spread out over a longer period (even for days) by the employment of a "drip" apparatus.

**Apparatus for Intravenous Infusion.**—In hospital practice, fluids for intravenous infusion are prepared with great care from pure chemicals and distilled water, and thereafter sterilized. Unless every detail in their preparation is scrupulously carried out, reactions may occur during and after their administration. They are transferred for administration to a large funnel or, better, to a flask container, the upper opening of which is kept loosely plugged by sterile cotton-wool or gauze to act as an air filter (Fig. 25). In general practice it is difficult to prepare uniformly satisfactory solutions, and it is highly advisable to procure them ready for administration from the firms<sup>1</sup> which specialize in their production; in these circumstances they are delivered to the vein from the container in which they are supplied. The rubber tubing which conveys fluid from container to vein requires special

preparation when it is new. It must be boiled in water for an hour, and thereafter its interior washed repeatedly by a stream of water; it is then ready to be sterilized for use. Needles are obtainable in a variety of designs.<sup>2</sup> They should be sharp, the bevel should be short, and it is convenient if they are fitted with flanges to facilitate their fixation; they should be made of rustless material. Cannulae may be of metal or glass; the former should be rustless, and both varieties are best constructed with a slightly bulbous tip, which permits a ligature to be securely tightened upon them. Recently long rubber cannulae have been introduced for use in "drip" methods; they

FIG. 25.—Diagram of Apparatus for Intravenous Infusion. A=sterile air-filter of cotton-wool or gauze; B= glass flask, 1 pint capacity; C=screw clip; D=glass "dripper"; E=glass connection; F=record fitting and needle (or cannula).

permit greater freedom of movement of the arm (or leg) after their insertion into the chosen vein.

A "dripper" is a glass tube (Fig. 26) into which the fluid is delivered drop by drop by a narrower tube, and it is connected to the container by a rubber tube on which is a screw clip. By the use of the clip the number of drops per minute can be varied; 40 to 50 is the usual rate. There should be a column of air between the drip-tube

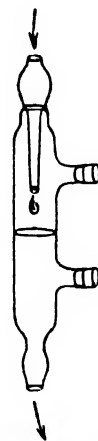


FIG. 26.—A "Dripper." By removing the upper cork air is allowed to enter and displace fluid which may have "backed up" to the inner tube.

<sup>1</sup> The Crookes Laboratories; Messrs John Bell & Croyden.

<sup>2</sup> Such as those of French, Kaliski or Keynes.

and the level of the fluid in the main tube; if this is lost by fluid "backing up" to the drip-tube, it can be restored by injecting, with aseptic precautions, a small quantity of air by means of a syringe and hypodermic needle passed through the rubber tubing immediately below the dripper. If a dripper of the type illustrated in Fig. 26 is used, the correction is more easily made by removing the rubber cork in the side limb.

An intravenous infusion should not be allowed to chill the patient; if given by the drip method any fluid is raised by the body to body temperature without any difficulty. Continuous infusions should be warmed before administration, and kept warm during it; when blood or serum or plasma is employed, care must be taken that it is not heated above 40° C. (104° F.).

A "head" of about 2 ft. is ample, except for those patients in whom the veins are in spasm due to shock, when the reservoir must be raised higher. The container may be held in a retort-stand; hung from a hook on the wall; tied to a screen; tied to a pole lashed to the head of the bed; or supported on a regular hospital type of adjustable stand.<sup>1</sup>

**Cannula Method.**—When the veins are collapsed, as in shock, or after severe hæmorrhage, and when the patient is so fat that they cannot be identified under the skin, a suitable vein must be exposed for the insertion of a cannula. When a single infusion is to be given, and the matter is urgent, as a rule the most prominent of the veins in both antecubital fossæ is chosen, or a long saphenous vein in front of one internal malleolus. When the drip method is to be used, the necessary immobilization of the limb is easier and less irksome to the patient if a vein on the flexor aspect of the forearm is chosen, or a sufficiently large vein on the dorsum of the hand, or a long saphenous vein.

An intradermal wheal of local anæsthetic is made over the vein at the selected level, about 0.5 c.c. of the solution is deposited in the tissues on each side of the vessel, and the area is compressed for a minute or two in order to distribute the anæsthetic. A tourniquet is applied to make the vein prominent, and an incision about 1 cm. long is made at right angles to the vein, while the skin is steadied by the fingers and thumb of the left hand. The wound is opened up and the vein cleared by inserting a closed small artery forceps on each side of the vessel in turn, and opening the points in a direction parallel to the vein. The closed artery forceps is then passed under the vein, and the tourniquet is released. A double strand of catgut is drawn under the vein by grasping its midpoint with the artery forceps, and the strand is divided so as to provide two ligatures of equal length. The distal of these is drawn to the distal part of the cleared vein, and used to ligate the vessel, the ends of the ligature being left long, and caught by an artery forceps. The proximal ligature is drawn to the proximal end of the cleared vein, and the first loop of a knot is loosely tied with it. Fluid is now allowed to flow through the infusion system and cannula until all air has been displaced, when the flow is stopped by clamping the rubber tubing with an artery forceps, about 15 cm. from the cannula. The cannula is laid on the sterile towel so that it can be picked up conveniently. The vein is now held up and steadied by the distal ligature, and an oblique nick is made into it with fine scissors—a good pair of manicure scissors answers

<sup>1</sup> A convenient and complete set, in a small case for ease of transport, is marketed by Messrs Archibald Young, of Edinburgh. It may be used for intravenous, subcutaneous or rectal administration of fluid.

very well. Care must be taken not to divide the vein completely, and yet to make a large enough opening; about half the circumference of the vein is adequate. Much the best instrument with which to hold the lips of the opening apart is a small sharp hook ("dural hook"); it is neater and more efficient than artery forceps or dissecting forceps. While the proximal lip of the opening is retracted with the hook, the cannula is inserted into the lumen of the vein; care must be taken to elevate the whole thickness of the wall of the vessel so that the glistening intima is displayed, otherwise it is possible for an inexperienced or careless operator to pass the cannula between the coats of the vein instead of into the lumen. The proximal catgut ligature is then tightened upon the cannula, and if the cannula has a "shoulder" the thread must be placed distal to this. The cannula may be fixed more firmly by tying the long ends of the distal ligature round it. As soon as the cannula is in position, the clamp is removed from the rubber tubing, and the flow of fluid started.

When a single infusion is to be given, 500 c.c. may be given in thirty to forty minutes, except in severe shock, when the first 500 c.c. of plasma must be given rapidly, in five to ten minutes. Before the last of the fluid runs into the vein, the cannula is withdrawn while the proximal ligature, the knot of which has remained half tied, is tightened to occlude the vein. Both ligatures are cut short, and the wound in the skin closed by a single stitch. A sterile pad and bandage are then applied.

**Needle Method.**—When a vein is readily accessible the infusion can be given through an "intravenous" needle. When the vein is prominent the needle can be inserted directly into it; or an intradermal wheal of anæsthetic may be made over the vein, the skin divided for a millimetre or two to expose the vein and the needle inserted into the exposed vein. The infusion apparatus (from which all air has been expelled) is connected to the needle by an adaptor, as soon as blood is seen to flow from the needle, and the fluid allowed to flow by unclamping the rubber delivery tube. When the infusion is completed the needle is withdrawn, and a sterile pad and bandage are applied to the site of puncture.

**Continuous Infusions.**—These are most satisfactorily given by the cannula method. A vein on the flexor aspect of the forearm, the dorsal aspect of the hand, or a long saphenous vein may be chosen. After the cannula is introduced and fixed in position, the part is bandaged so as to immobilize the terminal 15 cm. of the rubber delivery tube; if the patient is restless, a splint<sup>1</sup> may be necessary in addition; and if he is delirious, and an arm is being used for the infusion, the opposite hand must be controlled. The dripper is adjusted to deliver fluid at the appropriate rate. Thirty drops per minute will deliver a pint of fluid in about six hours and fifty drops per minute in about four hours.

In all such cases, and especially when the infusion is to be continued over a number of days, care must be taken that too much fluid is not administered. A record should be kept for each twenty-four hours in which intake is charted against output; the latter comprising the urine, water lost from the lungs and skin (about 1,500 c.c.), by vomiting and by diarrhoea. The appearance of œdema in the legs or about the sacrum is a warning either to discontinue the infusion or to reduce the rate of flow; and the bases of the lungs should be examined daily for signs of œdema. The period during

<sup>1</sup> For both arm and leg a moulded plaster of Paris splint is satisfactory.

which an infusion into a vein may be continued varies from patient to patient. Sooner or later the vein becomes the site of a non-infective phlebitis, ushered in by a feeling of local soreness; later the tissues in the immediate neighbourhood of the cannula become oedematous, and the skin reddened; and if the infusion is continued the redness and swelling spread proximally along the vein. The appearance of any of these complications is a signal to remove the cannula at once, and, if the infusion must be continued, to introduce the cannula into a vein in another limb.

### BLOOD TRANSFUSION

The intravenous infusion of blood in the treatment of hæmorrhage or anæmia was previously carried out by the direct method in which whole or unmodified blood was transferred from the vein of the donor to the vein of the recipient through a closed system of needles, tubing and a syringe in which coagulation was prevented by the use of a lubricant such as paraffin. This technique has now been superseded by the use of blood which is prevented from clotting by the addition of an anticoagulant. Blood is collected from the donor by venipuncture into a suitable container where it mixes immediately with the anticoagulant, and it is subsequently infused into the vein of the patient by a method similar to that described for intravenous administration of saline. The blood collected from the donor may be administered to the patient immediately as *fresh blood*. Alternatively, the container in which the blood has been collected may be hermetically sealed and placed in a refrigerator, where it can be kept until required (for a period up to 21 days) and then used as *stored blood*. Bottles of blood collected and stored in this way are now generally available in this country from one or other of the Blood Transfusion Services which have been established. Whether fresh or stored blood is used, certain precautions must be taken to ensure that the transfusion is effected without danger to the patient.

**General Precautions.**—The person from whom the blood is taken must be physically healthy: more particularly there should be no history or present evidence of any disease transmissible by blood such as malaria, infective hepatitis or syphilis. Whenever possible the Wassermann reaction of the donor's blood should be proved to be negative: this is always done in the case of blood from the Transfusion Services.

The blood must at all times be protected from contamination by organisms by the most rigid asepsis. The sterilization of apparatus should be by heat, because any antiseptic will damage the blood, but the apparatus must not be hot when used and the blood must never be warmed above 40° C. (104° F.) because of the danger of denaturing the proteins. In storage the temperature should be about 4° C. and should never be as low as 0° C. because this will damage the cells. Blood removed from storage should be used within 6 or 8 hours and should be discarded if the zone of hæmolysis in the supernatant fluid has extended more than halfway up the plasma layer. Anything more than a slight degree of hæmolysis in stored blood may be due to the presence of infection. Finally, blood must never be infused until it has been proved by suitable tests to be compatible with the blood of the patient.

**Testing Compatibility of Blood.**—In all cases the practitioner administering the blood to the patient is responsible for ensuring that the blood

used is compatible. Where facilities are not available for determining the type of the patient's blood, or when the practitioner is not experienced in the necessary tests, he should delegate this responsibility to the expert at the Blood Bank. The expert requires for tests both the corpuscles and the serum (or plasma) of the recipient. These are most easily provided by sending to him 3 to 5 c.c. of whole blood in a test-tube: this blood is obtained from the patient by venipuncture. If it is not convenient to withdraw blood from a vein, a smaller quantity obtained by pricking a finger or ear may be made to serve by drawing it up into two or three capillary glass tubes and sealing their ends in a flame. Each sample must be carefully labelled with the patient's name before despatch to the Blood Bank.

The expert will determine the patient's blood group by tests on the corpuscles (which he obtains by teasing the clot), and he will carry out a direct compatibility test between the patient's serum and the cells of the blood which he selects from the Bank. He will then be able to provide blood certified compatible with the prospective recipient. This blood must not, of course, be used for any other patient without further tests.

In hospital practice the house physician or house surgeon should normally be able to accept responsibility both for determining the blood group of the patient and performing the direct compatibility test. An invariable request for Group O blood is not in the best interests of the patient (for reasons explained below), nor fair to the Blood Bank, whose supply of Group O blood is limited. The Blood Bank should be informed of the group to which the prospective recipient belongs and will supply blood of the same or a compatible group, depending on the supplies available. The basis and technique of the tests are described in the following paragraphs.

*Blood Groups and Compatibilities.*—Many different blood groups have been distinguished and the number is steadily increasing, but in transfusion practice we are concerned mainly with the four main groups which have been designated AB, A, B and O.<sup>1</sup> The bloods are so named because of the presence or absence of two agglutinogens named "A" and "B" in the cells. Corresponding to these agglutinogens are their homologous antibodies or agglutinins, named " $\alpha$ " and " $\beta$ " respectively. The agglutinin is present in the serum of any blood from whose cells the corresponding agglutinin is absent. This reciprocal arrangement is shown in the following table :—

TABLE III

Blood Group (and Agglutinin in Cells).	Agglutinin in Serum.
AB	None
A	$\beta$
B	"
O	and $\beta$

<sup>1</sup> The nomenclature (Universal) used here is that now adopted as standard in this country. It should be noted, however, that the groups are frequently also numbered according to the system of Moss, viz., AB (I), A (II), B (III) and O (IV). Care must be exercised in reference to American literature, where the numbers are sometimes different, after the system of Jansky, viz., AB (IV), A (II), B (III) and O (I).

It will be seen that when any two whole bloods of different groups are mixed, some incompatibility will result: the cells of at least one of the two bloods will contain an agglutinin which corresponds to an agglutinin in the other serum. In the laboratory, therefore, the mixture of whole blood samples will result in some agglutination unless the bloods are of the same group. In giving blood transfusions, however, it is found that the effect of the serum of the donor on the red blood cells of the recipient can be neglected in routine practice; only the effect of the serum of the recipient on the corpuscles of the donor need be considered. This means that the blood infused does not always require to be of the same group as that of the patient: it must, however, be of a group whose cells will not be agglutinated by the serum of the patient. Reference to the table will accordingly show that:—

Group AB blood can be given only to a patient of Group AB.

Group A blood can be given to patients of Groups AB and A.

Group B blood can be given to patients of Groups AB and B.

Group O blood can be given to patients of any group.

These generalizations must, however, be qualified by the statement that sub-groups exist and may occasionally result in incompatibilities which are not allowed for in this scheme. They are therefore used only as a guide in the selection of the donor blood, which must still be proved suitable by a direct compatibility test as described below.

*Determination of Blood Group.*—Reference to Table III will show that the group of any given blood can be determined by testing its corpuscles separately against two sera, one of which contains only agglutinin  $\alpha$  and the other only agglutinin  $\beta$ . Such sera are obtainable from bloods of Groups B and A respectively, and are provided commercially in phials or capillary tubes for the purposes of the test. The sera provided by reputable firms have been proved by test to have a high titre of the agglutinin required. To preserve this high titre they should be stored in a refrigerator. The test is conducted as follows:—

A suspension of the cells of the blood to be typed is prepared by mixing one drop of the blood with 2 or 3 c.c. of isotonic saline in a small test-tube.

Two clean microscope slides are marked "A" and "B" respectively. On each a drop of the appropriate serum is placed. To each drop is added a drop of the cell suspension of the blood to be grouped and the drops are thoroughly mixed, a clean glass rod or a new wooden match being used for each to ensure that there is no transference of agglutinins from one slide to the other. If agglutination is going to appear, as a rule it does so rapidly, but an interval of fifteen minutes should be allowed before the slides are finally read. During this time they should be rocked at intervals and evaporation should be prevented by placing the slides on damp filter paper and covering them by inverted glass dishes when they are not being handled. Agglutination is usually obvious to the naked eye, but in doubtful cases the cells may be scrutinized under a lower power of a microscope. If a microscope is used, rouleaux formation should not be mistaken for agglutination. According to the result, the blood group of the person being tested can be determined thus:—



TABLE IV

Agglutination of unknown Cells by		Unknown belongs to
Group A Serum.	Group B Serum.	
+	+	Group AB
-	+	„ A
+	-	„ B
-	-	„ O

*Direct Test of Compatibility.*—When a donor or a bottle of stored blood has been selected as suitable for transfusion to a particular patient on the basis of the above tests, it is still necessary to prove compatibility by a direct test. This is not only advisable as a double check to prevent mistakes, but is essential because of the existence of certain sub-groups which occasionally result in incompatibility. The omission of such a direct test is not justifiable except in circumstances of extreme urgency and difficulty, as in transfusions conducted near the battlefield in war.

The direct test of compatibility must be made between the cells of the donor and the serum of the recipient. Reactions between the cells of the recipient and the serum of the donor may be ignored in all but exceptional cases. It is misleading, therefore, to observe the effect of mixing drops of the two whole bloods. This, as already explained, will result in some agglutination unless the two bloods are of the same group and will not give the information required. The test should be carried out as follows :—

A suspension of the cells of the donor is made by mixing one drop of blood obtained by finger prick in 2 c.c. of isotonic saline in a test-tube. If stored blood is to be used, cells for this test are usually provided in a small test-tube attached to the blood bottle.

The serum of the patient may be obtained by withdrawing a few c.c. of blood from a vein and allowing it to clot in a test-tube. Venipuncture is, however, unnecessary and often undesirable, and the serum is as easily obtained by drawing blood from a finger prick into a capillary glass tube. The tube is sealed at both ends in a flame and the serum given time to separate or obtained by centrifuging.<sup>1</sup>

A drop of the recipient's serum (which is obtained from the capillary tube by breaking off the appropriate length) is then placed on a microscope slide, a porcelain tile or white saucer, and mixed with a drop of the cell suspension from the donor. The mixture should be watched for at least 15 minutes, evaporation being prevented as described above and the slides rocked to and fro at frequent intervals. If no agglutination occurs, the donor's blood may be used for transfusion: if any agglutination is seen the blood is not suitable. When several pints of blood are to be administered to the same patient, they should all be of the same blood group, as bloods of different groups which are individually suitable for the patient may be incompatible with each other.

<sup>1</sup> A centrifuge may be improvised by fastening the tube(s) by sticking plaster to a blade of the fan of a motor car, or to the "rim end" of a spoke of the back wheel of an upturned bicycle.

*The Rhesus Factor.*—Recent work has shown that in certain circumstances an additional factor may be responsible for incompatibility in transfusion. Various antigens which have been named Rhesus or Rh factors (so called because they were first detected in the red cells of the Rhesus monkey) are present in the red cells of about 85 per cent. of human beings. The remaining 15 per cent. are Rh-negative, and in certain circumstances these individuals may develop in their sera homologous antibodies to Rh antigens and become "Rh-sensitive." This occurs particularly when an Rh-negative woman becomes pregnant with an Rh-positive foetus (the Rh factor is inherited as a Mendelian dominant). The Rh factor passes the placental barrier and stimulates the formation of a specific antibody in the maternal blood. This in its turn may pass into the foetal circulation and there destroy the red cells. The foetus may be killed, leading to stillbirth (hydrops foetalis), or it may be born with grave anæmia of hæmolytic type and marked hypertrophy of the marrow (icterus gravis neonatorum, erythroblastosis foetalis, etc.). Both the mother and the child are Rh-sensitive, and if they are to be transfused, Rh-negative blood must be used.

Antibodies to the Rh factor may also be developed in the blood of any Rh-negative individual who has already received several transfusions of Rh-positive blood.

In practice, therefore, we must consider the Rh factor in any woman who is or has been pregnant, in any foetus born with severe hæmolytic anæmia, and in any individual who has previously received numerous transfusions. Blood Transfusion Centres now keep a supply of Rh-negative blood for use in these cases, but supplies are limited and its use is not justifiable unless it is proved to be necessary. The tests for Rh factor and Rh antibodies can be done only by experts, and a sample of the blood of the patient who is suspected of being Rh-sensitive should be sent to the Blood Bank (2 or 3 c.c. of clotted blood in a test-tube or a few sealed capillary tubes containing whole blood are sufficient). The expert will determine whether the blood is in fact Rh-negative and contains Rh antibodies, and will supply Rh-negative blood if this is necessary.

**Administration of Blood.**—*Stored Blood.*—The Blood Transfusion Centres collect blood from suitably selected donors of known blood group. This blood is prevented from coagulating by mixture with a solution containing sodium citrate, and is stored in refrigerators until required. It can generally be used with safety up to three weeks from the date of withdrawal (which is shown on the label on the blood bottle), but the older the blood when it is used, the less lasting will be the benefit to the patient. The corpuscles of blood which has been stored for more than a few days will survive in the circulation of the recipient for a relatively shorter time, and though such blood will be entirely serviceable for the treatment of shock due to hæmorrhage, it will be less useful in the treatment of chronic anæmia. When large amounts of blood (one litre or more) are to be given to a patient, the urine should be rendered alkaline before transfusion by oral administration of 30 gr. (1.8 gm.) of sodium citrate and 30 gr. (1.8 gm.) of sodium bicarbonate four-hourly (see p. 942).

The blood is supplied in a standard M.R.C. bottle hermetically sealed by a screw cap with a rubber diaphragm inside. A small test-tube containing a quantity of the same blood is usually attached for direct compatibility tests as described.

The blood should be inspected for evidence of excessive hæmolysis in the supernatant plasma (see p. 933).

If it is to be administered slowly, it is not necessary to warm it in any way. If it is to be administered rapidly, it is desirable to warm it slightly. Standing at room temperature for an hour or two will be sufficient, or the bottle can be immersed in warm water for 15 to 20 minutes. This water should never be warmer than 40° C. or a temperature which the practitioner's hand can bear with complete comfort. The blood should be mixed only by gentle inversion of the bottle once or twice before the screw cap is removed.

A pre-sterilized packet containing the attachments necessary for giving the blood is supplied with the bottle. This apparatus is already assembled for use, and consists of a rubber bung with long air inlet tube (occluded at its outer end by a rubber cap) and short outlet tube covered by a wire gauze filter; the outlet is connected by a short piece of rubber tubing to a "dripper," from which a longer length of tubing (about 3 ft.) ends in an attachment for needles of the "Record" type. The packet also contains a screw clamp and a test-tube containing both a needle for vein puncture and a metal cannula for tying into the vein if required.

In assembling the apparatus it is of paramount importance to ensure that no part of it which is to be in contact with blood or the patient's tissues is touched by the hand or allowed to touch anything which is not absolutely sterile. If it is handled with care, the assembly may be done with ordinarily clean and dry hands. The sterilized paper packet is opened and the rubber bung grasped at its base between finger and thumb with care that no part above is contaminated. The glass tubes and wire gauze filter are then inserted into the blood bottle from which the screw cap has been removed, and the rubber bung is firmly impacted. The bottle is now inverted, the air inlet is opened by removing the glass rod, and the system of tubing, dripper, and connections is filled with blood so that no bubbles of air remain. The screw clamp provided is placed on the tubing between the bottle and the dripper (see Fig. 27). The needle is then inserted into a suitable vein and the transfusion

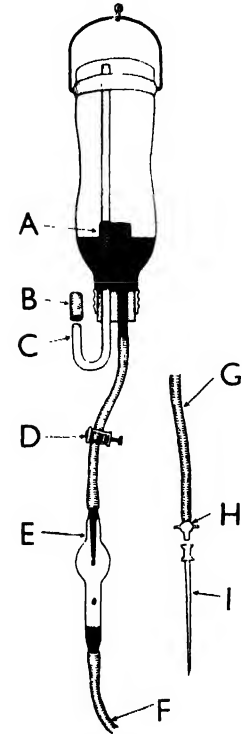


FIG. 27.—Diagram of Apparatus for Blood Transfusion: Standard Type supplied by Blood Transfusion Services. A=wire gauze filter; B=rubber cap (sometimes with glass rod) to occlude C=inlet tube; D=screw clip to control rate of flow; E=glass "dripper"; F and G=rubber tubing about 3 ft. long; H=record type fitting for I=needle or metal cannula.

started by opening the screw clamp to allow the required flow as judged from the dripper. When a continuous transfusion is desired and several pints of blood are to be infused slowly over a period of hours or days, it may be desirable to tie the cannula or blunt needle into a vein as described for the continuous administration of saline (p. 931). When the blood is running very slowly the cells will settle in the reservoir and this should be agitated gently from time to time.

Sometimes, as in severe shock, the veins of the recipient are so collapsed

that puncture with a sharp needle is difficult or impossible. Even when a cannula has been tied into the vein this spasm may prevent an adequate rate of flow of the blood. A greater head of pressure is most safely obtained by raising the reservoir to a higher level. Warmth applied to the limb in the course of the vein by a fomentation, a rubber hot-water bottle or an electric blanket may help to release the spasm. In extreme cases pressure must be obtained by pumping air into the air inlet tube of the blood bottle as with a Higginson's syringe or sphygmomanometer cuff. When this is done, certain additional precautions are essential. The air pumped in must be filtered through a glass connection filled by sterile cotton-wool; the rubber bung must be very firmly fixed in the neck of the bottle in case it blows out, and no pressure is to be applied after the bottle is two-thirds empty because of the danger of massive air embolus if the fluid finally runs out and is followed by the compressed air.

*Fresh Blood.*—In certain circumstances, as when the medical indications call for the transfusion of fresh blood, or when blood is not available from a Transfusion Centre, the practitioner may have to arrange to select a suitable donor and withdraw the blood himself.

The donor's physical health must satisfy the requirements already described (p. 933), and his blood must be proved compatible by grouping and direct testing with the patient's serum. In emergency, or when commercial grouping sera are not available, the direct compatibility test must suffice. If possible, a donor should not give blood for transfusion immediately after a meal, especially if the recipient is known to be allergic to any foodstuff.

**Collection of Blood for Transfusion.**<sup>1</sup>—The donor should be recumbent. A pad is placed behind the elbow, and the skin over and around a suitable antecubital vein is sterilized and isolated. The cuff of the sphygmomanometer, or some other form of tourniquet, is placed round the arm to impede the venous return and make prominent the chosen vein. Two or three drops of local anæsthetic are injected into the skin over the vein at the site to be punctured. After a wait of two or three minutes, a minute nick (about 2 to 3 mm.) is made in the skin with the point of a sharp scalpel. The apparatus for puncturing the vein consists of a needle of wide bore (e.g., a French's needle) attached to about 12 in. of wide (e.g.,  $\frac{1}{4}$  in.) rubber tubing, the whole being sterilized by boiling.<sup>2</sup> The blood is received into a sterile graduated jar, which contains sterile (3·8 per cent.) sodium citrate solution as an anticoagulant. This may be prepared from the pure chemical and freshly distilled water, the solution being sterilized by boiling or in the autoclave; or a sterile concentrated solution may be purchased,<sup>3</sup> and diluted with sterile distilled (pyrogen-free) water. For each 90 c.c. of blood to be transfused, 10 c.c. of 3·8 per cent. citrate solution are required; it is convenient to start with 50 c.c. of the citrate solution in the receiver and to withdraw about 450 c.c. of blood. Before the needle is inserted into the vein, needle and tubing should be washed through with sterile citrate solution. The vein is punctured through the nick in the skin and the needle is held in position while the blood is flowing; to avoid clotting in the needle

<sup>1</sup> Some Blood Transfusion Centres supply a simple withdrawal set already sterilized for use, consisting of an M.R.C. bottle with the necessary attachments.

<sup>2</sup> The needle is wrapped in lint or gauze before boiling.

<sup>3</sup> British Drug Houses Ltd. market ampoules containing 1 gm. of sodium citrate in 4 c.c. of distilled water. The contents of two ampoules, made up to 50 c.c. with distilled water, are sufficient for a transfusion of 500 c.c.

or tube, the flow of blood should be maintained at a steady rate by adjustment of the tourniquet and by directing the donor to clench and unclench his hand at intervals of about ten seconds. The blood is meanwhile thoroughly mixed with the citrate solution in the receiving receptacle by rotating it, or by stirring with a sterile glass rod. When the required quantity of blood has been collected, first the tourniquet is released and then the needle is withdrawn. The puncture is firmly covered with a sterile pad of gauze, and the arm is bandaged. The removal of 450 c.c. of blood from a healthy adult is seldom attended by any unpleasant sequel, but it is advisable to keep the donor recumbent for 15 to 20 minutes after completing the withdrawal.

If apparatus such as is used in the Blood Transfusion Services is available, the technique of giving fresh blood will not differ in any way from that described for stored blood except that it will not be necessary to warm the blood. More commonly the blood will have been collected into an open receptacle such as an enamel jar and must be administered with a flask or funnel and tubing as is described for infusion of saline. If the blood has been well mixed with citrate solution during collection, there should be no clots and a filter is not essential, as it is when stored blood is used. It is, however, a wise precaution to pour the blood into the reservoir through three or four layers of sterilized gauze.

**Infusion of Concentrated Red Cells.**—The infusion of concentrated red cells raises the hæmoglobin level without adding to blood volume, and it is therefore of value in the rapid correction of anæmia before operation, and possibly in certain forms of aplastic anæmia. Group O blood, which has been kept for a week in the ice-box, is employed, the supernatant plasma and white cells being withdrawn aseptically from two bottles. The contents of two bottles of red cells are then mixed and directly infused after dilution, if necessary, with 3·8 per cent. citrate solution.

**Intramedullary Transfusion.**—Recent experience has demonstrated the value of the medullary cavity for transfusion of citrated blood or infusion of saline or other fluids, particularly in obese or shocked patients with collapsed veins. The sternum is the most convenient bone except in small children in whom the upper end of the tibia may be preferable.

The technique of introducing the needle into the sternum is similar to that employed in sternal puncture for diagnostic purposes. A point is chosen in the median line about the level of the upper border of the third rib, the skin, subcutaneous tissues and periosteum are infiltrated with local anæsthetic and a Salah sternal puncture needle is introduced obliquely upwards into the sternal cavity. The stylet of the needle is withdrawn, a "Record" syringe attached to the needle, and a small quantity of marrow juice aspirated. The syringe is then removed and the adaptor of the transfusion apparatus, previously set up, is connected to the needle and the transfusion begun. In most cases the control clamp may be opened to its full extent, the rate of flow being governed by the ability of the marrow to absorb fluid; under such conditions the rate varies from 50 to 150 drops per minute. After the needle has been inserted, the procedure is painless and transfusions or infusions may be maintained without discomfort over periods of many hours. Strict asepsis must be maintained.

Difficulty may arise when the needle is pushed in so far that its bevel abuts on the inner table of the sternum; a slight readjustment of the needle will result in a satisfactory flow. Occasionally the flow of transfused

blood may gradually become slower, and eventually stop; usually it can be restarted by disconnecting the drip apparatus, aspirating the medullary cavity with a syringe, and reconnecting the drip.

Occasionally patients are encountered in whom attempts at sternal transfusion are unsuccessful owing to relative impermeability of the marrow cavity, but they are rare enough to warrant a trial of this technique when the usual methods of transfusion present difficulty.

**Administration of Plasma.**—All Blood Transfusion Centres now prepare and provide bottles of blood plasma.<sup>1</sup> It may be supplied in liquid form and with pre-sterilized apparatus, exactly as for blood transfusion. Sometimes it is dried<sup>2</sup> and supplied in the form of a yellow powder: it must then be reconstituted for administration by the addition of sterile distilled water. The quantity of distilled water which must be added is generally indicated by a mark on the bottle: about 400 c.c. is required for 30 gm. of the powder. The distilled water used for reconstitution must be pyrogen-free—specially prepared for intravenous administration. The bottle must be shaken for about five minutes to effect complete solution, and the reconstituted plasma *should be used at once*.

Plasma infusion is particularly indicated in certain cases of shock, such as severe burns, when hæmoconcentration is present. It can also be used with benefit in cases of shock due to hæmorrhage when whole blood is not immediately available. The technique of administration is the same as in blood transfusion. Tests of compatibility are not required.

**Reactions to Transfusion of Blood or Plasma.**—Minor reactions may occur during the transfusion for several reasons, and usually manifest themselves in a shiver followed by fever and headache or nausea. This may be due to unduly rapid administration of stored blood, to impurities in the citrate solution or to lack of cleanliness<sup>3</sup> or sterility in the apparatus. If the reaction is slight, the rate of delivery should be reduced to 15 or 20 drops a minute: if the symptoms do not abate or pass off within five minutes, the transfusion should be stopped. If the reaction is initiated by a definite rigor, the flow should be stopped immediately. The patient is treated by warmth externally, hot drinks and a sedative such as 10 gr. (0.6 gm.) aspirin and 5 gr. (0.3 gm.) Dover's powder in slight cases, or  $\frac{1}{4}$  gr. (16 mg.) of morphia in more severe cases. If the patient is collapsed, an injection of 8 minims (0.5 c.c.) of 1:1,000 adrenaline hydrochloride solution should be given subcutaneously.

When blood is being transfused for chronic anæmia, the patient is likely to have an initial low blood volume with high cardiac output and myocardial degeneration. In these patients there is great danger of overloading the circulation by running the transfusion too fast, and an early reaction may take the form of acute cardiac failure evidenced by collapse with a fast

<sup>1</sup> Some Transfusion Centres also supply serum on request. Serum is used in the same way as plasma and has no particular advantage.

<sup>2</sup> The only advantage of dried plasma (or serum) is that it can be kept longer (even for several years), and under any condition of temperature. Wet plasma (or serum) can be kept at room temperature for several days and in a refrigerator for many months, but it is safer not to use it more than six months after preparation.

<sup>3</sup> The rubber tubing and other attachments which are used for transfusions are meticulously cleaned in the Blood Banks before being sterilized for re-use, but it is extremely difficult to remove dried blood from the inside of a rubber tube and therefore most important that the practitioner using the apparatus should wash it through carefully with cold water immediately after use while the blood is still fluid.

thready pulse and perhaps dyspnoea. The transfusion must be stopped immediately and the patient laid flat in bed.

Occasionally a reaction of an allergic type occurs, with pain in the chest, dyspnoea and circulatory collapse. Its nature is recognized from the development of an urticarial rash which may be widespread. Such reactions are most likely to occur if the same donor is used for a second transfusion. They are seldom serious, but if recognized while the transfusion is in process the flow should be stopped. Adrenaline (0.5 c.c. of 1:1,000 solution) is given subcutaneously and followed by  $\frac{1}{4}$  gr. (16 mg.) of morphia. The injection of adrenaline may be repeated later as the urticaria may persist for 24 or 48 hours.

Rarely, minor reactions occurring after completion of the transfusion are due to the presence of an unusually high titre of agglutinins in the serum of the blood transfused, causing some agglutination of the recipient's cells if these belong to a group other than O. Such reactions are very seldom severe and are so rare that, as has been explained, they are not usually considered in the compatibility tests. They are treated by warmth, sedatives and adrenaline as described above.

Severe reactions are due to mistakes in cross matching resulting in the rapid agglutination of the transfused red cells. This agglutination is followed by hæmolysis of the donor cells. Soon after the start of the transfusion the patient becomes restless and complains of lumbar pain or pain in the chest and head. A rigor, severe dyspnoea and then respiratory and circulatory failure may follow rapidly. If the patient survives, fever follows and later jaundice; hæmoglobinuria and oliguria are evident. The precipitation of pigment in the renal tubules may still lead to anuria, uræmia and death. If the transfusion is stopped at the first signs of such a severe reaction, and the urine is promptly rendered alkaline, a fatal outcome can often be prevented. Adrenaline and morphine are given subcutaneously and the patient is kept warm. Rapid alkalization of the urine should be assured by the intravenous injection of 100 c.c. of a 2 per cent. solution of sodium bicarbonate.<sup>1</sup>

All urine passed by the patient should be kept and measured and a fluid chart of intake and output made. The blood urea nitrogen should be estimated daily. The alkalinity of the urine is maintained by giving sodium citrate and sodium bicarbonate, 30 gr. (1.7 gm.) of each, four-hourly by mouth with large quantities of water. This dose can be reduced after the first day but the urine should be kept alkaline for at least one week. If anuria occurs in spite of alkalization, an isotonic solution of sodium sulphate (4.285 per cent.) should be infused intravenously at the rate of about 30 drops per minute. When anuria persists for more than 24 hours, peritoneal dialysis may be undertaken to control the uræmia. If it persists for two days, it may be justifiable to decapsulate one kidney.

Whenever a reaction has occurred during the transfusion of blood or plasma supplied by a Transfusion Centre, the remainder of the contents of the bottle should be preserved with precautions against organismal contamination, and returned with full particulars to the Blood Bank for examination.

Sometimes, after the transfusion of several pints of stored blood without immediate reaction, jaundice develops within 24 to 48 hours. This is due

<sup>1</sup> An alternative intravenous injection consists of 10 c.c. each of isotonic sodium lactate and a saturated solution of sodium bicarbonate. Ampoules of these can be obtained ready for use from Crookes Laboratories.

to hæmolysis of a portion of the transfused red cells because of their increased fragility after storage. It is treated in the same way as jaundice following transfusion of incompatible blood.

A late reaction to transfusion of blood, or more commonly to the infusion of plasma, may occur up to 120 days after the administration in the form of homologous serum jaundice (see p. 924).

### INTRADERMAL INJECTION

Occasionally it is necessary to introduce small amounts of fluid into the skin. This may be needed to test for sensitivity on the part of the patient towards serum, bacterial products or extracts of certain animal and vegetable substances; or the procedure may be a therapeutic one (*e.g.*, sera and egg-albumin in hæmophilia, bee venom in rheumatic disease). The finest of needles should be employed, with a short bevel on its point. A small syringe containing the appropriate quantity of fluid is attached to the needle, and its contents are introduced into the skin where it is hairless, usually on the flexor surface of a forearm. The accurate placement of the fluid is secured by passing the needle, bevel downwards, into the skin at a very acute angle; if the point of the needle is correctly placed, the injection causes blanching of the skin over a small circular area.

### HYPODERMIC INJECTION

By this route are administered (1) certain drugs, (2) vaccines, (3) sera, and (4) certain hormones, *e.g.*, insulin.

1. **Drugs.**—These may be already in solution in ampoules. If they are in tablet form, the appropriate dose is dissolved in about 1 c.c. of sterile water. The solution may be made in a china egg-cup, which is boiled in water in a pan from which the required amount of sterile water is removed with a syringe, also boiled in the pan; or if the syringe is already sterile, the necessary amount of water may be boiled in a tablespoon over a spirit lamp or gas jet. The needle should be the finest procurable, and sharp; the ideal is to use a fresh needle for each injection. Areas suitable for hypodermic injections are indicated in Fig. 28. The skin at the selected point is cleansed with spirit, a fold of it is picked up with the finger and thumb of the left hand, and the needle attached to the syringe is plunged rapidly into the *loose subcutaneous tissue* at the extremity of the fold. The piston is then withdrawn slightly, to ensure that the point of the needle is not in a venule; if blood does not enter the syringe, its contents are injected, and the needle withdrawn. Hypodermic injections should never be given into an inflamed area, or into an area which may contain lymphatics draining an inflamed area (*e.g.*, *not* into the arm on the side of a whitlow).

2. **Vaccines.**—These are often supplied in bulk, in bottles with a thin

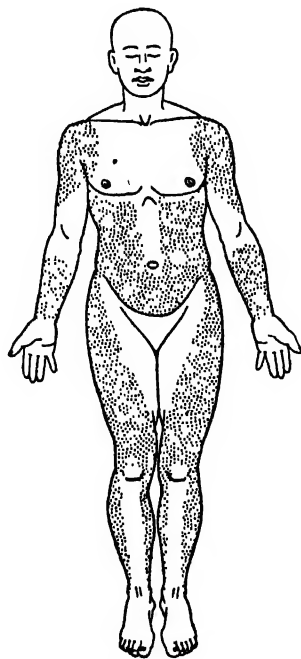


FIG. 28.—The Shaded Areas may be used for Hypodermic Injections.



rubber cap. The bottle is well shaken, and the cap is sterilized with spirit; if the bottle is new, a layer of paraffin wax may have to be removed from the rubber cap. The piston of the syringe is then withdrawn to the level of the dose desired; the needle is plunged through the rubber cap into the bottle, which is held *inverted*; air is expelled into the bottle by pushing the piston "home," and the equivalent dose of vaccine is then withdrawn into the syringe.

3. **Sera.**—These are withdrawn from the containing ampoule and introduced under the skin, through a long needle of medium bore. When the amount of serum is large, the injection is best made under the loose skin of the pectoral or interscapular regions; and the point of the needle may be shifted occasionally, to avoid depositing a "blob" of serum at any one point.

4. **Insulin.**—(See p. 353).

### INTRAMUSCULAR INJECTION

The intramuscular route is chosen for the administration (a) of certain preparations (*e.g.*, penicillin or liver extract); (b) of suspensions of insoluble drugs (*e.g.*, mercury); and (c) of some sera (*e.g.*, antitetanic serum) when it is desired to provide a depot of serum. A long (5 to 8 cm.) needle is employed; it should be of as fine a bore as is consistent with the viscosity of the injected material, which may be reduced if necessary by warming the container to about 105° F. If the material is irritating to the subcutaneous tissues (mercurial suspensions) the syringe should be filled either directly, without a needle, or through a second needle.

Intramuscular injections can be made into the gluteal muscles, above a line joining the anterior superior iliac spine and the fold of the buttock (Fig. 30), or into the muscle mass on the lateral side of the thigh. When intramuscular injections are to be repeated at regular intervals the site should be varied, as by using alternate sides or different zones previously mapped out on the sides of the thighs. Single injections of small quantities of sera may be introduced into a deltoid or pectoralis major muscle. When the gluteal region or the lateral side of the thigh is chosen, the patient should lie on the opposite side. The skin is sterilized and steadied by the forefinger and thumb of the left hand; the needle is held in the forefinger and thumb of the right hand, and is plunged through the skin perpendicularly, with a sharp stabbing movement, directly into the muscles. If its point impinges on the bone, the needle should be withdrawn slightly. It is then held in position with the forefinger and thumb of the left hand, and the charged syringe is attached to it. Gentle suction is applied to ensure that the point of the needle is not in a blood vessel; if it is correctly placed, the injection is slowly and steadily completed. If an irritating substance has been injected, before the needle is removed it is rotated once or twice in its long axis in order to cleanse it. Thereafter the area is massaged firmly for a minute or two, to ensure even dispersion of the injected material.

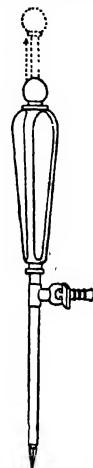
### PARACENTESIS OF THE ABDOMEN

This is indicated when ascites embarrasses movement, respiration or the heart's action.

The point usually chosen for the puncture is in the median line, equidistant from umbilicus and symphysis. The bladder is emptied, if necessary by catheter. If the abdomen is hairy it is shaved. The patient should be in a semi-reclining position, so that the fluid gravitates towards, and the intestines away from, the lower abdomen; and before the abdomen is tapped a broad binder (or roller towel) should be placed round the upper part of the abdomen. This is tightened as the fluid escapes, and thus faintness from the reduction of intra-abdominal pressure is prevented. Either of two methods may be employed.

**By Trocar and Cannula.**—An instrument of the "piston" type is the most convenient; this has a cannula with a side limb, which opens into the cannula only when the trocar is withdrawn beyond the junction (Fig. 29). To the side limb rubber tubing is attached, long enough to reach a receptacle by the side of the bed. A scalpel with a narrow blade is also necessary. The abdomen is cleansed and the selected point isolated by sterile towels. An intradermal wheal of local anæsthetic is raised here, and the deeper tissues are also infiltrated. A small cut is made through the skin, of such a size that it will admit the point of the trocar and stretch to accommodate the cannula. The cannula, with trocar in position, is then pushed slowly through the abdominal wall; the right forefinger is kept firmly upon it to guard against its plunging too far into the peritoneal cavity. When resistance is overcome, the point of the instrument has reached the cavity. The trocar is withdrawn, and fluid will flow through the side limb. Not infrequently a loop of bowel floats up and obstructs the cannula so that the flow ceases. It can be restarted by moving the cannula up and down, or from side to side. Occasionally a flake of lymph blocks the cannula; this can be dislodged by the cautious reinsertion of the trocar. As the abdominal swelling decreases the binder is tightened; but if the patient complains of faintness the flow is temporarily stopped until he recovers. When the flow finally ceases the cannula is withdrawn, and the tiny wound sealed with collodion.

**By Southey's Tube.**—This fine tube removes fluid more gradually, and therefore the patient does not require constant attention throughout the drainage. The cannula is connected to a length of thin rubber tubing which reaches a receptacle beside the bed. The tubing is stretched over the mouth of the cannula, and the trocar is inserted *through* the stretched tubing; when the trocar is withdrawn after puncture of the abdominal wall the opening in the tube closes. Often the flow of fluid will begin at once; if it fails to do so, a syringe may be attached to the distal end of the tube and gentle suction applied in order to establish syphon action. The cannula may be left in position for many hours.



(By courtesy of Down Bros. Ltd., London.)

FIG. 29.—Trocar and Cannula for Paracentesis of the Abdomen.

### ASPIRATION OF THE PLEURAL CAVITY

This may be necessary either as a diagnostic procedure, to determine the physical, cytological and bacteriological nature of a pleural effusion, or as a therapeutic procedure, to withdraw from the cavity a considerable

amount of fluid (for example, in metapneumonic empyema, in cases of cardiac or renal failure or to evacuate a traumatic hæmothorax).

Although it is occasionally necessary to choose an interspace which lies directly over the site of the effusion, as determined by clinical and especially radiological evidence, as a rule the puncture is made in the eighth intercostal space, in the posterior axillary line, and nearer the ninth than the eighth rib in order to avoid the intercostal nerve and vessels. The patient may be either in a sitting position or propped up near the edge of the bed in a semi-reclining position, with the arms folded. After the usual preliminary preparation and isolation of the area, an intradermal wheal of local anæsthetic solution is raised at the point selected for the puncture, and 2 c.c. of the solution is then deposited in the deeper tissues; the needle should be made to impinge on the lower rib. It is well to wait a few minutes in order to give the anæsthetic time to act, and to reach the vicinity of the pleura.

**Removal of a Sample.**—A rather wide-bore, short-bevelled needle is attached to a 5 c.c. syringe, and the needle is then pushed slowly into the pleural cavity. If a little negative pressure is maintained in the syringe, fluid will flow at once when the cavity is reached, and the needle should not be introduced further. When the syringe is full the needle is withdrawn, and the sample transferred to a sterile test-tube with a closely fitting rubber cork. The puncture is then sealed with collodion.

**Aspiration as a Part of Treatment.**—When it is decided to remove a quantity of fluid, a 50 c.c. syringe is useful. This is connected to the aspirating needle by 6 in. of stout rubber tubing fitted with adaptors. The aspirating needle and small syringe are used as described to ascertain the proper depth; the large syringe is then coupled to the needle.<sup>1</sup> It is *slowly* filled; the tubing is then pinched, or clamped with a spring clip, and the syringe is disconnected and emptied. The cycle is repeated until (1) fluid is not obtained, or (2) the patient complains of or shows respiratory embarrassment, often heralded by short paroxysms of coughing. It is seldom wise to withdraw more than 15 oz. of fluid at one time, unless the fluid is being replaced by air (see p. 145). The needle is then withdrawn and the puncture sealed with collodion. It is a useful plan in cases of empyema to retain from each aspiration a corked test-tube almost full of pus; these are placed in a rack, and the process of "thickening" of the pus can be followed by comparing the levels of cellular sediment in the tubes.

An alternative method is to employ a 20 c.c. syringe to which is coupled a three-way adaptor. One channel of the adaptor leads by way of 6 in. of rubber tubing to the aspirating needle; to the other channel is attached sufficient rubber tubing to reach a receptacle for the aspirated fluid. The junction of the channels is controlled by a stopcock, turning of which allows the syringe to be alternately filled from the chest and emptied into the receptacle. This method is also employed when the aspirated fluid is to be replaced by air; after the syringe is emptied it is filled with a somewhat smaller quantity of air, which is introduced slowly into the pleural cavity. This procedure prevents any sudden disturbance of mediastinal relationships; in favourable cases the lung expands slowly as the air is absorbed.

<sup>1</sup> Messrs Down Bros. sell a useful contrivance for maintaining the fixed position of the needle. It consists of a rubber vacuum "sucker" which sticks to the skin, and carries an arm in which the needle rests.

The procedure is repeated as often as clinical and radiological examination indicate the need for it.

When it is desired to follow the aspiration by injecting penicillin into the pleural cavity, this should be done before removing the needle. A clean syringe is charged with the solution of penicillin. After a final confirmation that the needle point is still in the pleural space, the aspirating syringe is replaced by the penicillin syringe with care not to disturb the position of the needle, and the fluid is injected.

**Dangers of Pleural Aspiration.**—Very rarely puncture of the pleura is immediately followed by *pleural shock*, a condition characterized by extreme cardiac and respiratory failure. If this happens the needle must be withdrawn; the remedial measures include warmth, artificial respiration if necessary, and the subcutaneous injection of 0.5 c.c. (8 minims) of 1 : 1,000 adrenaline hydrochloride, with 2 c.c. of nikethamide.

### PARACENTESIS OF THE PERICARDIUM

In each case the skin is cleansed and sterilized and then anæsthetized by intradermal and subcutaneous novocain over the area selected for puncture, as in performing a pleural paracentesis. Where pus is suspected, a wide-bore needle (2 mm.) may be necessary, but, in general, a medium bore will suffice (about 1 mm.). The length of needle required depends largely on the site of puncture. The following sites are usually employed: (i) in the fifth left interspace, outside the apex beat but inside the limit of cardiac dullness; (ii) in the fourth left interspace about 1 in. from the sternal margin (far enough from the bone to avoid the internal mammary artery which descends in this region); (iii) in the angle between the ensiform cartilage and the lowest ribs, the needle being directed upwards and backwards to reach the pericardial sac; (iv) from the back, with abducted scapula, in the mid-scapular line in the seventh or eighth intercostal space. Of these, the first two are those most generally used, and appear to be devoid of risk. The penetration of the heart muscle by the needle is of no consequence provided that large coronary vessels be not punctured; this is an unlikely accident from a needle inserted outside the apex beat, or over the area of the right ventricle lying 1 in. to the left of the sternum, which is relatively devoid of large vessels. The epigastric and posterior routes are occasionally preferable when a loculated effusion has to be reached; in both these fluid is reached at a deeper level than when an anterior puncture is performed and more complete drainage can be carried out. When large quantities of fluid are being removed the rate of withdrawal should be slow, to avoid the risk of dangerous pressure changes in the pericardium or heart.

### LUMBAR PUNCTURE

This consists in the introduction of a hollow needle into the subarachnoid space in the lumbar region, a procedure which is employed for both diagnostic and therapeutic purposes. A lumbar puncture needle must be of fine bore, with a sharp, shortly bevelled point, and a closely fitting stylette; it is so marked that the line of the bevel can be visualized by looking at the base of the needle. Occasionally a needle of large bore is needed to withdraw thick exudate, but

even "thick" liquids (such as sera and lipiodol) can be introduced through a fine needle if the ampoule containing the liquid is warmed in a bowl of hot sterile water to a temperature of 110° F., and the barrel of the syringe is kept warm by covering it with relays of gauze swabs soaked in the hot water.

**Technique.**—In most cases the puncture must be performed with the patient in bed, but if his surroundings or size permit, it is more easily carried out as he lies on a firm surface, such as a kitchen table or operating table. He should lie on his left side, and a small pillow is placed under his head in order to keep the cranial and spinal parts of the subarachnoid space at the same level. The patient then bends his head slightly forwards, and clasps

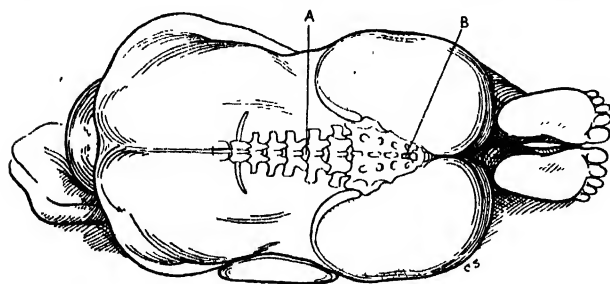


FIG. 30.—Patient in position for Lumbar Puncture. A, Site for lumbar puncture; B, Site for epidural injection. The stippled areas are suitable for intramuscular injections.

his knees with his hands, so as to arch his back and thus open out the spaces between the spinous processes of the lumbar vertebræ (Fig. 30). Only in the most unruly or unco-operative of adults is an anæsthetic needed, and usually a child can be gently but firmly held in the same position.

Inhalation anæsthesia interferes with the accurate measurement of cerebrospinal fluid pressure, and if this information is important, papaveretum-scopolamine for an adult and chloral hydrate for a child should be tried first.

Usually the needle is inserted between the spines of the third and fourth lumbar vertebræ, a level which corresponds to the point where a line joining the highest points of the iliac crests crosses the spinal column. After the usual preparation, and with a towel in position, this point is identified with the left thumb and an intradermal wheal of local anæsthetic is raised in the median line with a fine hypodermic needle. A larger needle is used to infiltrate the deeper tissues in a forward and slightly cranial direction; the needle should never be sunk to its full extent, for needles break at the junction of shaft and adaptor, and if the patient moves suddenly, a fully inserted needle may snap here, and disappear below the skin. After two or three minutes, to give time for local anæsthesia to develop, the spinal needle is inserted through the same hole in the skin, and with its bevel in the same plane as the spine,<sup>1</sup> and pushed slowly forwards and cranially with the right hand while its direction is maintained by the forefinger of the left, which rests on the skin. At a distance from the surface which varies with age and build (in the average adult, 4 to 5 cm.) the needle is felt to overcome a certain resistance—that of the ligamentum subflavum between the laminæ. If it is pushed onwards for 0.5 cm. it will have pierced the dura and entered the spinal subarachnoid space.

**Difficulties in Lumbar Puncture.**—Lack of co-operation on the part of

<sup>1</sup> Held thus it will separate, rather than sever, the longitudinally directed fibres of the dura. On its withdrawal, the small dural slit closes without leaking.

the adult patient should be met with only in those who are semiconscious or delirious; in the majority of cases firm holding, careful local anæsthesia and patience will enable the puncture to be completed. The same plan is as a rule successful in children. If the bed is soft, allowance must be made for the tilt of the patient's body, the needle being directed a little downwards as well as forwards and cranially. When the needle impinges on bone before entering the spinal canal, it is usually found to have been pushed in too caudal a direction; it must be withdrawn for 3 cm. before being advanced more cranially. When the spine is arthritic, great patience in searching may be required to find an interval between the laminæ; and the puncture may have to be attempted in another lumbar interspinous space, for example, between the second and third spinous processes. If the fluid which drops from the needle is blood-stained, a little should be allowed to run down the wall of a test-tube held on a background of white gauze. If the tint becomes progressively less deep, it is likely that a small vessel has been opened by the needle, and readings of pressure may be taken. Later two or three samples are collected in a series of tubes, and those that are clear (or less deeply tinted) used for investigation. When the cerebrospinal fluid already contains blood, the tinting will persist, and may be assumed to be of diagnostic importance. The importance of admixture of blood may be assessed later, by allowing the sample to settle, or by centrifuging it. When the blood results from local trauma, the supernatant fluid is clear<sup>1</sup>; but when it has been derived from a previous subarachnoid hæmorrhage the supernatant fluid is yellowish or red. If fluid does not flow, and it is reasonably certain that the point of the needle is in the subarachnoid space, it should be slowly rotated, a manœuvre which is usually followed by a flow of fluid as the result of the clearing of a nerve root which previously blocked the aperture.

**Cerebrospinal Fluid Pressure.**—Investigation of the fluid pressure in the subarachnoid space is usually important and sometimes of essential diagnostic value. It is estimated in terms of millimetres of itself, and the estimation must be made before taking a sample. The needle is connected by means of a three-way stopcock and adaptor,<sup>2</sup> and a short length of rubber tubing, to a manometer of glass graduated in centimetres; the whole apparatus must be sterilized by autoclaving or boiling. The stopcock allows the operator (1) to close the lumen of the needle, (2) to allow cerebrospinal fluid into the manometer, or (3) to allow cerebrospinal fluid to flow directly into a sample tube. The manometer is held so that the zero mark is at the level of the needle. Pressure readings are useless unless the patient is relaxed and breathing quietly, and it may be necessary to wait for this situation and to secure it by encouragement. Normally the fluid shows oscillations up to 0.5 cm. with each beat of the pulse, and up to 1.0 cm. with each respiration; the mean is taken as the initial pressure.

If the subarachnoid space above the level of the needle is free from obstruction, then variations in its pressure will be at once transmitted to the manometer. The presence of variations of pressure with pulse and respiration is evidence of free communication. The situation may be investigated further by the manœuvre of Queckenstedt. Normally the compression by an assistant of both internal jugular veins for four seconds

<sup>1</sup> Such a mixture may show lysis of red cells if the sample is transmitted to the laboratory by post.

<sup>2</sup> Either Greenfield's or Adson's pattern is convenient.

(the patient having been previously warned) leads to an increase in pressure in the intracranial space of anything up to 30 cm., and if obstruction is absent this is at once reflected by a rise in the manometric reading; and the manometric pressure falls abruptly when the jugular compression is released. If obstruction (*e.g.*, a spinal tumour) is present, then when jugular compression is applied, the manometric pressure may—

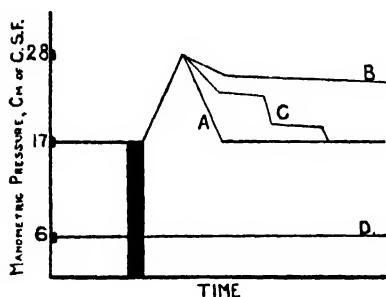


FIG. 31.—Diagrammatic Representation of Manometric Response to Jugular Pressure. The black block represents compression of the internal jugular veins for four seconds. A, normal response; B, new higher level; C, "stairway" fall; and D, lack of response (complete block).

1. Remain stationary (complete block).
2. Rise, but remain at a higher level when jugular compression is released (partial block).
3. Rise or fall jerkily ("stair" response) when the jugular pressure is applied or released (partial block).

When block is present, the "initial pressure" is low; but manual compression of the abdomen will be followed by a rise

in pressure, even when response to jugular compression is absent.

The information that may be obtained from investigation of the pressure of the cerebrospinal fluid is indicated in Fig. 31, and in Table V.

TABLE V

Condition.	Pressure. Mm.	Colour	Coagulum	Cells. Per Cn. Mm.	Protein. Per Cent.	Glucose. Per Cent.	Chlorides Per Cent.	Wassermann
Normal . . . . .	80 to 175	Clear	None	0 to 3 (S.L.)	0.015 to 0.025	0.04 to 0.08	0.72 to 0.73	Neg.
Acute meningitis . .	+ + +, to 1,000	Turbid to purulent	Present	+ + + (P.)	0.5 +	Dim or absent	Nor. to 0.6	"
Tuberculous meningitis .	+ +	Clear to turbid	Us (fine)	+ + (L.), occas + (P.)	0.05 to 0.5	"	Nor to 0.55	"
Acute syphilitic meningitis .	Us. + to + +	"	Occas. (fine)	"	0.04 to 0.4	Us. nor.	V. slt. dim.	Pos., 85%
Vascular neurosyphilis .	Nor. to +	Clear	None	Nor. to + (L.)	0.15 to 0.5	Nor.	Nor.	" 75%
Tabes dorsalis . . .	Nor.	"	"	Nor. to 200 (L.)	Nor. to 0.1	"	"	" 80%
Dementia paralytica .	Nor. to +	"	Occas (fine)	"	0.25 to 0.5	"	"	" 100%
Benign lymphocytic meningitis . . . . .	"	"	Rare	25 to 500 + (L.)	0.02 to 0.07	"	"	Neg.
Acute anterior poliomyelitis .	"	"	Occas. (fine)	+ + P., later + L.	0.02 to 0.35	"	"	"
Epidemic encephalitis .	Us. nor., rarely +	"	None	10 to 500 (L.)	Nor. to 0.08	"	"	"
Disseminated sclerosis .	Nor.	"	"	Us. nor., rarely + (L.)	Nor., or + (0.15)	"	"	"
Polyn neuritis ("neuritis") .	Nor. to +	"	"	Nor. to +	Us. +, to 0.75	"	Nor. to dim	"
Aseptic meningel reactions .	Us. + to + +	Clear to turbid	Occas.	To 10,000 (P.)	0.02 to 0.2	"	"	"
Cerebral abscess . . .	"	Clear to purulent	"	+, to 800 (P., L.)	+, to 0.2	Nor., occas. dim.	Nor.	"
Supratentorial cerebral tumour .	"	Clear, occas. yellow	None	Nor. to 150 (L.)	Nor to 2.0	"	"	"
Infratentorial cerebral tumour .	"	"	"	"	Nor to 0.5	"	"	"
Spinal cord tumour . .	Low (Block)	Clear to yellow	Occas.	Nor., occas. +	0.04 to 3.5	"	"	"
Spontaneous subarachnoid hæmorrhage .	Us. + +	Bloody xanthochromic	None	+ +, R.B.C.	0.02 to 1.0	Nor., occas. dim.	"	"

dim. = diminished. L = Lymphocyte. nor. = normal. P. = Polymorph. us. = usually.

**The Collection of Samples.**—When manometric readings have been made, fluid is allowed to drip slowly into a tube or series of tubes for further examination. Tubes should be chemically clean and sterile, and should be fitted with stoppers of rubber. Fifteen cubic centimetres of fluid is sufficient

for all routine analyses, but when a space-occupying intracranial lesion is present or is suspected, the withdrawal of fluid should be stopped at an amount which does not reduce the manometric pressure by more than one-third of the initial reading. Otherwise the only *contraindication* to lumbar puncture is certainty of diagnosis without the assistance it may afford.

The number of tubes into which the sample is divided depends upon the tests which are desired, and the laboratory or laboratories to which samples are to be sent. Thus information may be desired as to (1) the chemical, (2) the cytological, (3) the bacteriological, and (4) the immunological properties of the fluid (Table V). Three separate samples should satisfy the most exacting of laboratory colleagues.

After a lumbar puncture the hole in the skin should be sealed with a pledget of cotton-wool soaked in collodion or with sterile plaster, and the patient should be kept in the recumbent position for twenty-four hours in order to avoid the unpleasant sequel of "lumbar puncture headache."

NOTE.—If the inexperienced operator be so unfortunate as to have a needle break off under the skin, he should at once mark the puncture by a needle scratch and, if possible, obtain skilled surgical aid. An incision is made in the median line between the two adjacent spinous processes, the two erector spinæ muscles are separated, and the interspinous tissue (and broken portion of the needle) are grasped between the widely opened jaws of a curved artery forceps applied in the line of the spine. The forceps is then closed and withdrawn.

### CISTERNAL PUNCTURE

For diagnostic or therapeutic purposes the *cisterna magna* of the subarachnoid space may be tapped through the atlanto-occipital ligament. This procedure has the advantage over lumbar puncture that it is not attended by the possibility of headache, that the exudate in meningeal infections may be more easily withdrawn and the appropriate sera introduced, and that radio-opaque substances (iodized oil, B.P.) may be introduced at the cranial end of the spinal canal. It is, however, potentially more dangerous than lumbar puncture because of the proximity of the *medulla oblongata*.

**Technique.**—The head and neck are shaved below the level of the bases of the mastoid processes and prepared surgically. The patient lies in the left lateral position, the head being raised by a pillow to the level of the cervical spine, and well flexed to open up the interval between occipital bone and atlas. A point is identified in the median line immediately above the spine of the atlas, or, in a thick-necked patient, where a line joining the tips of the mastoid processes crosses the spine. The skin is anæsthetized by intradermal infiltration of local anæsthetic. A spinal puncture needle is then introduced and pushed forwards and cranially, under the control of the left index finger, till it impinges on the occipital bone. It is then withdrawn for 2 cm., the point directed more caudally, and the needle pressed forwards through the atlanto-occipital membrane and dura, which are felt to "give," into the *cisterna magna*; normally in an adult this lies at a depth of 4 to 6 cm. from the skin. When the needle is disconnected, fluid drops slowly or may be withdrawn by a syringe. Its properties may be investigated as are those of fluid obtained by lumbar puncture. If this route is used to inject fluids into the subarachnoid space, great care must be taken during the injection that pressure on the piston of the syringe does not push the needle onwards, for this mistake may result in injury to the *medulla oblongata*. Throughout an injection the depth to which the needle is allowed to penetrate should be controlled by the thumb and fingers of the left hand.



When the needle is withdrawn the puncture is sealed with cotton-wool and collodion.

### EPIDURAL INJECTION

By this procedure fluid is forced between the dura and the bony wall of the lower part of the spinal canal. A lumbar puncture needle is used for the injection, and it is introduced between the cornua of the last piece of the sacrum, through the roof of the spinal canal which is here ligamentous.

**Technique.**—The patient lies face downwards, preferably on a firm surface, with a large pillow under the pelvis. A piece of gauze is placed between the buttocks to prevent the antiseptic from reaching the anus or genitals, and the skin over the sacrum, coccyx and buttocks is cleansed. The position of the sacral cornua is found by palpation, and an intradermal wheal of local anæsthetic is raised between them. The tissues down to the bone are then infiltrated with a somewhat larger hypodermic needle, which can be felt to pierce the ligament bridging the cornua, and two or three minutes are allowed for the anæsthetic to take effect. A lumbar puncture needle is then introduced through the puncture already made in the skin, and pushed onwards and cranially at an angle of about 45 degrees with the horizontal, and in the median line, until it is felt to pass through the ligamentous roof of the canal, and come to rest on the posterior surface of the body of the sacrum. The base of the needle is then depressed between the buttocks, to alter its direction, and it is pushed cranially for about 3 cm. along the sacral canal. At this stage its position is verified by making the point impinge on the bony roof of the canal (Fig. 30). A 20 c.c. syringe is then filled with sterile saline, or 0.25 per cent. procaine solution, and fitted to the needle. The plunger is withdrawn slightly, to make sure the point of the needle is not in a vein; and the contents of the syringe are slowly injected. Very little pressure is needed, and if the plunger has to be forced, the point of the needle is not correctly placed in the sacral canal, but lies between the sacral laminae and the skin, in the origin of the erector spinæ.<sup>1</sup> When the first 20 c.c. have been injected, it is well to pause for a minute or two; the needle is then slowly pushed onwards in the sacral canal, nearly to its full extent. A second and even a third 20 c.c. of solution are then introduced; as the beneficial effects of the injection may be due partly to its disruptive effect, the writer makes a practice of injecting the final 10 c.c. under pressure. During the injection (which is usually done for sciatica) the patient may complain of exacerbation of pain in the affected leg.

The needle is withdrawn, and the puncture in the skin sealed with a pledget of cotton-wool soaked in collodion. The patient may then turn on his back, but should rest in this position for half to one hour before leaving. When procaine solution has been used, its correct placement may be verified by the appearance of perianal analgesia within fifteen to twenty minutes.

**Difficulties.**—Although the injection is usually easy, the sacral cornua may be distorted, and it may take patience and gentle searching with the needle's point to enter the canal. The ease with which fluid may be injected is the best guarantee that the needle has been correctly placed. Occasionally in sensitive patients tachycardia follows the injection of procaine, and the patient must remain at rest till the pulse-rate returns to normal.

Epidural injection may be utilized to aid in the diagnosis of a tumour

<sup>1</sup> If the injection is persisted in when the needle is in the latter position, a palpable and visible lump forms on the back of the sacrum.

compressing the theca below the level of the interval between the third and fourth lumbar vertebræ. Lumbar puncture is performed in the usual way, and manometric readings are taken. A needle is then introduced into the sacral canal, and fluid is slowly injected. If the canal is unobstructed, the injected fluid displaces a certain volume of cerebrospinal fluid, by compressing the theca, and the pressure in the lumbar manometer rises. If the sacral canal is obstructed by an intradural or extradural tumour, fluid can be introduced only with difficulty, and the pressure does not rise in the lumbar manometer.

### ASPIRATION OF JOINTS

The method of puncturing the cavities of joints for diagnostic and therapeutic purposes is shown in the diagrams and described in their accompanying captions.

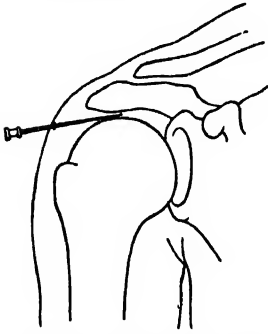


FIG. 32.—*Shoulder joint.* From immediately distal and somewhat posterior to the tip of the acromion process, the needle passes medially and a little cranially, over the humeral head.

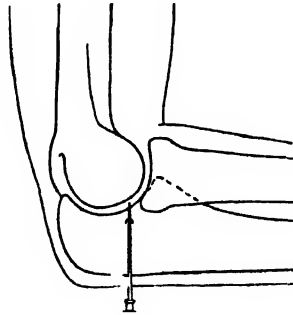


FIG. 33.—*Elbow joint.* With the forearm at right angles, and midway between pronation and supination, the needle passes anteriorly from a point immediately proximal to the head of the radius.

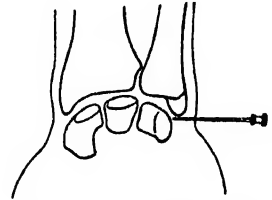


FIG. 34.—*Wrist joint.* From a point immediately distal to the styloid process of the ulna, the needle passes laterally.

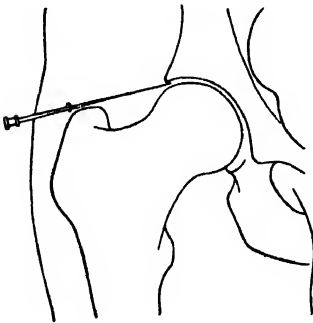


FIG. 35.—*Hip joint.* From a point immediately proximal to the mid-point of the upper border of the greater trochanter, the needle passes medially and slightly cranially, along the neck of the femur.

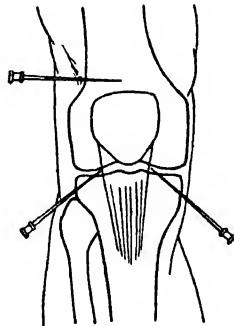


FIG. 36.—*Knee joint.* The needle may pass from either the medial or the lateral side (1) into the suprapatellar pouch, or (2) into the joint on either side of the ligamentum patellæ.

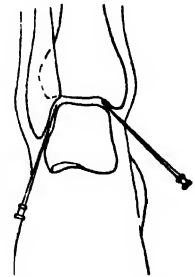


FIG. 37.—*Ankle joint.* From a point immediately distal to the tip of either malleolus, the needle passes cranially, and towards the median line of the tibia, between the malleolus and the talus.

J. R. LEARMONTH.  
A. G. R. LOWDON.

## OXYGEN THERAPY

Though a very great improvement was noted in the course of the war years, both in equipment and in appreciation of its value and proper use, there were till recently few potent therapeutic agents which, both in hospital and in private practice, were in general used to such little effect as oxygen. Considerable misunderstanding existed regarding the indications for its use, its administration was frequently delayed till the prospects of benefit were negligible, and the methods employed were generally both wasteful and inefficient. Too often it was given by tube and funnel, with totally negative effects, or a nasal catheter (which is quite efficient when properly used) was employed under conditions of maximum discomfort to the patient and minimum efficiency. The common method of fixing the catheter to the cheek with adhesive strapping caused considerable discomfort in a man from traction on the growing beard, and irritated an ill patient beyond endurance. The delivery of the gas from the cylinder through a wash-bottle filled with warm water, acting as a rough flow-meter, led generally to rates of flow too low for effective action. Finally, there persisted for too long the custom of giving oxygen intermittently, for a certain number of minutes in each hour. This practice is illogical and harmful, and has been likened by Haldane to "dragging a drowning man to the surface once a minute." Oxygen therapy to be fully effective must be continuous, so long as indications for it persist.

To-day, thanks it would appear to the exigencies of "total war," efficient oxygen apparatus is widely distributed over the country, and even small hospitals are well equipped. It is especially noteworthy that not only in teaching hospitals but in many others, apparatus exists capable of dealing simultaneously with a fair number of cases requiring oxygen, either by branched distributors from large cylinders serving six or more beds, or by including piping to each bed in the plumbing, so that oxygen is as readily available for any case as electric light or radio. This is of value especially when special wards are set aside for pneumonia, and is well suited for the treatment of gas casualties should such occur in numbers from industrial accident or enemy action.

**Indications.**—The giving of oxygen might be expected to be of value in cases where there is a deficiency of oxygen in the arterial blood, *i.e.*, in anoxæmic states. It should be realized, however, that not all forms of anoxæmia are benefited by oxygen inhalation. In severe uncomplicated anæmias, for example, anoxæmia exists, but such hæmoglobin as remains in circulation is fully saturated with oxygen as it leaves the lungs, and the plasma holds its full complement in solution. The oxygen tension of the blood is therefore normal, and additional oxygen in moderate concentrations (up to 50-60 per cent.) in the respired air does not increase that in the blood to any significant degree. When very high concentrations of the gas are obtainable (over 90 per cent. in the *alveolar* air) the amount held in solution in the plasma does increase significantly. These concentrations are attainable with modern simple apparatus, and are used in treatment of cases of traumatic shock, etc. Again, peripheral cyanosis is no certain indication that oxygen therapy will be of value, for the blood leaving the lungs may be fully oxygenated and the cyanosis may be due to slowing of

the peripheral blood flow or to admixture of venous with arterial blood as in some cases of congenital heart disease. In those cases, on the other hand, where blood leaves the lungs only partly saturated with oxygen, increase in the oxygen content of the respired air raises its partial pressure in the alveolar air, and improves the oxygen saturation of the arterial blood. Such defective oxygenation, or *anoxic anoxæmia*, arises whenever there is interference with the passage of air to and from the lungs, or with the gaseous interchange in the alveoli. It can arise very readily in the pneumonias, where a number of factors favour its production. If part of the blood in the pulmonary circulation flows through vessels in airless consolidated lung, the blood in the pulmonary veins will not be fully oxygenated. Again, a film of watery or fibrinous exudate over the endothelial surfaces of air-containing alveoli interferes with the gaseous exchange between blood and alveolar air, and the rapid shallow breathing which is common in pneumonia further interferes with the efficiency of pulmonary ventilation. Patchy atelectasis and exudation, as in capillary bronchitis and broncho-pneumonia, lead to a similar state of defective oxygenation of the arterial blood, as does pulmonary congestion and the cedema of cardiac failure. In all these states the timely and efficient administration of oxygen is of great value.

A further important indication for the use of oxygen is in the treatment of carbon monoxide poisoning. The affinity of this gas for hæmoglobin is such that a concentration of 0.05 per cent. of carbon monoxide in the respired air will lead to the conversion of more than half the circulating hæmoglobin to the carbon monoxide compound. A very low concentration of the gas thus leads to a great reduction in the hæmoglobin available for oxygen carriage. The compound of carbon monoxide and hæmoglobin is stable, and will only dissociate to form free carbon monoxide and hæmoglobin in the presence of a high concentration of oxygen. This dissociation may therefore be accelerated in clinical practice by increasing the oxygen content of the respired air, *i.e.*, by oxygen therapy, which comes to be an important part of the resuscitation of patients poisoned by this gas.

Oxygen therapy has been employed in the treatment of cases of heart failure and of emphysema. In the latter, raising the oxygen in the alveolar air relieves cyanosis to some extent, but from the chronic nature of the disease it is obvious that oxygen therapy is of limited value. It is not feasible to give oxygen by mask or other means for prolonged periods, and in practice oxygen therapy in cases of emphysema is only applicable during periods of excessive oxygen want, as in intercurrent attacks of bronchitis or broncho-pneumonia. In heart failure, likewise, oxygen may be given as a temporary measure, and may be of value to tide the patient over some crisis such as an attack of pulmonary cedema, acute failure following coronary thrombosis, or pulmonary infarction. Under experimental conditions patients have been treated in the oxygen chamber for a long time (*e.g.*, six weeks), but it is not feasible to give oxygen continuously for such periods with ordinary clinical appliances, and its use in cases of chronic heart failure is therefore of limited value. It is noteworthy that oxygen, even when efficiently given, may yet fail to relieve the dyspnœa of cardiac failure. Cardiac dyspnœa appears to be caused by many factors, of which noxæmia is not the most important.

The success or failure of oxygen therapy in general cannot be assessed solely by the abolition or persistence of dyspnœa, a point emphasized by

Christie,<sup>1</sup> for oxygen lack is a factor of little significance in the production of respiratory embarrassment. Physiologists likewise are agreed that oxygen lack does not cause dyspnoea, a fact well attested by the experiences of those who have subjected themselves to rarefied atmospheres. A patient may stand in desperate need of oxygen without being dyspnoeic, and conversely a patient who is both dyspnoeic and anoxæmic may derive great benefit from oxygen therapy as regards his anoxæmia and yet may still remain dyspnoeic from other causes.

It is sometimes desirable to increase the depth of respiration, as for example in cases of pneumonia with rapid, shallow breathing. As already noted, this type of breathing aggravates greatly the anoxæmia arising from other causes. Again, after anæsthesia with chloroform or ether, deep respiration accelerates the rate at which the drug is excreted by the lungs and shortens the post-operative period of anæsthesia. Deep breathing during the recovery period from such anæsthesia also helps to prevent the plugging of bronchi with sticky mucus, and lessens the risk of post-operative pulmonary collapse. Deep respiration, with efficient ventilation of the bases of the lungs through the action of the diaphragm, also lessens the risk of hypostatic pneumonia in elderly subjects suddenly confined to bed by such accidents as fracture of the femur, etc. In all these conditions the inhalation of a low concentration (5 to 10 per cent.) of carbon dioxide will stimulate respiration considerably, and is therapeutically effective.

For clinical use oxygen is supplied in cylinders containing the desired percentage (5 or 10 per cent.) of carbon dioxide, and the mixture is given in the same way as simple oxygen (*e.g.*, by simple face mask or nasal tube).

**Requirements.**—Some idea of the quantity of oxygen required may be gained from consideration of the following points. The tidal air (air inspired and expired at each breath) is about 500 c.c., and with a respiratory rate of 20 per minute this entails a pulmonary ventilation rate of 10 litres per minute. In the case of a patient who is in need of oxygen therapy the total minute ventilation is frequently double this figure, namely, 20 litres per minute. This represents an intake of 4 litres of oxygen every minute, since air contains 20 per cent. of that gas. To raise the oxygen content of the alveolar air to double the normal might be expected, therefore, to require about 4 litres per minute flow of additional oxygen. Since with many methods of administration (nasal catheter, etc.) the gas flows continuously and is wasted during expiration, *i.e.*, during approximately half the respiratory cycle, even higher rates of flow may be required.

**Methods.**—Many varieties of appliances are available for the clinical administration of oxygen of all degrees of complexity and efficiency. Before reviewing the individual methods it is well to consider the general principles underlying their design. There are four main factors to be studied: efficiency, cost, comfort in use and simplicity in working.

The estimation of efficiency, though possible to some extent by clinical observation, is capable of exact determination only by alveolar air analyses. It is the partial pressure of the oxygen in the alveolar air which determines the amount taken up by the blood, and this pressure depends on the percentage of oxygen in the alveolar air. Normally the alveolar air contains about 14 per cent. of oxygen, which corresponds to a partial pressure of

<sup>1</sup> *Lancet*, 1938, 2, 876.

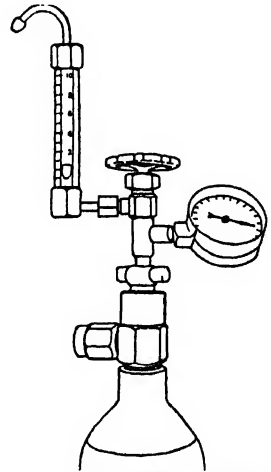
about 100 mm. Hg. An efficient method of oxygen therapy should at least double, or preferably treble, this value, and should raise the alveolar oxygen content to about 40 per cent. The quantity of oxygen per minute required to effect this increase varies considerably with the method of administration. With some methods, *e.g.*, the old tube-and-funnel apparatus, it is frankly impossible to raise the oxygen content of the alveolar air to anything like the essential 40 per cent. level, while with others the required figure can be reached with varying ease. There are available various methods of providing oxygen-enriched atmospheres.

At one limit stands the all-steel airtight oxygen chamber, so expensive that only the wealthiest of institutions can afford to install it, and at the other the simple nasal catheter costing a few pence. For all practical purposes, however, the administration of high concentrations of oxygen can be carried out by the use of relatively simple appliances; a concentration up to 45 per cent. can be obtained by using the nasal catheter and its variants, and up to 95 per cent. by the B.L.B. mask. Those alone will be described, as they are efficient, reasonable as regards initial cost and expense in use, and simple in principle. Oxygen chambers and tents though efficient are expensive and demand an elaborate nursing technique. They have in general been superseded by the B.L.B. mask, except for infants and young children and for post-operative cases in thoracic surgical practice. The old-fashioned tube-and-funnel method represents merely a waste of time and oxygen and should never be used.

A simple flow-meter should be considered an essential part of an apparatus for administration of oxygen, together with a fine-adjustment valve for controlling the supply. A simple and compact form of valve and flow-meter is illustrated in Fig. 38, the cost of such an apparatus being about £4. Without a flow-meter the rate of delivery of the gas is mere guesswork, and efficient working of any apparatus is unlikely.

A word of warning is necessary regarding the danger of fire, ignorance of which may lead to serious accidents: objects which merely smoulder in air burst into flame in high concentrations of oxygen (*e.g.*, cigarettes); fire may also be caused by lubricating with oil the valves of high-pressure oxygen cylinders. This latter is usually warned against specifically by the manufacturers in printed legends on the cylinder-head.

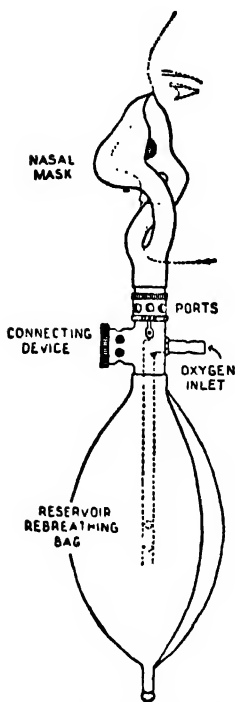
*The Nasal Catheter.*—Two varieties of intranasal tube are in use, of which the nasal catheter is the more familiar. The catheter should be of soft rubber, size No. 9, and should be lubricated with a bland emollient. Benzocaine ointment is useful for this purpose, combining lubrication with anæsthetic properties. The tube is usually inserted till the tip touches the back of the nasopharynx, and then withdrawn slightly ( $\frac{1}{4}$  to  $\frac{1}{2}$  in.). The free end should be carried upwards to the forehead, and fixed there either by adhesive strapping or preferably by a forehead-mirror head band and light clip. The usual practice of affixing the catheter to the cheek with adhesive plaster is undesirable, particularly in men, from the discomfort produced



(By courtesy of Cozeters.)

FIG. 38.—Valve and Flow-meter for Administration of Oxygen.

through traction on the growing beard. The other practice so often seen, of fixing the tube to the pillow with a safety-pin, is equally undesirable, since a slight movement of the patient's head may then draw the catheter from the nostril.



(By courtesy of the "Lancet.")

FIG. 39.—The B.L.B. Mask.<sup>1</sup>

The Tudor-Edwards spectacle frame is an elaboration of the nasal catheter. The oxygen is led into a metal tube, bent to rest on the bridge of the nose and retained in place by the spectacle earpieces. From this bridge (which is of soft metal and adjustable to the features) two lateral tubes pass downwards, one for each nostril. From the ends of those fine rubber catheters pass into the nostrils, the apparatus being, in effect, a double-nasal catheter. This apparatus is more comfortable and efficient than the simple nasal catheter and is quite cheap. With either type the maximum content of oxygen in the alveolar air is of the order of 40 per cent., and to attain this rate of flow almost 6 litres per minute are required. This may be accompanied by some discomfort, due to the force and drying effect of oxygen impinging on the mucous membrane, which can be greatly relieved by several simple stratagems: (a) The catheter should have several additional lateral openings cut on it, as this dissipates the force of the oxygen stream. (b) The nasopharynx and oropharynx should be sprayed at frequent intervals with liquid paraffin from an efficient atomiser. This greatly reduces the feeling of rawness and discomfort frequently complained of in those parts. (c) In the case of the simple catheter it may be inserted into the two nostrils alternately.

*The B.L.B. Mask.*—This mask, devised in 1938 by Boothby, Lovelace and Bulbulian of the Mayo Clinic, is at once the most efficient, most economical and most comfortable device for the therapeutic administration of oxygen. The type in most common use delivers the oxygen through a small nasal mask, but there is an additional model with an oronasal face-piece for use where nasal obstruction exists.

From a small nasal mask, fitting snugly against nose, cheeks and upper lip, pass two tubes, one on either side of the mouth, the two uniting over the lower part of the chin into a single tube. This latter connects with an aluminium tube, "the connecting device," to the lower end of which, in turn, a rubber bag of about 700 c.c. capacity is attached.

The connecting device has three small ports drilled at its upper end, and those can be covered or exposed by rotation of a metal collar in which corresponding holes are drilled. Farther down the oxygen inlet tube is attached, and diametrically opposite an expiratory valve is fixed. To the inner end of the oxygen inlet tube is attached a piece of rubber tubing so that the oxygen is delivered into the bag. For sterilization the makers recommend that each part be washed with soap and water and rinsed before boiling for three minutes. It is advisable to support the rubber

<sup>1</sup> The model in current production has a simple connecting device without ports.

parts on a wire screen to prevent their coming in contact with the overheated bottom of the utensil. After boiling they are hung up to drain and dry. No antiseptic should be used.

The mask is fitted to the patient's face and held in position by two rubber straps, which clasp behind the head, passing either above or below the ears, as may be most comfortable. During this procedure the oxygen should be flowing freely (6 litres) so that there is no resistance to inspiration; the flow of oxygen can be adjusted later. It will be found that in the majority of cases breathing will be mainly through the nose; mouth breathing of moderate degree, eating and speaking do not reduce significantly the efficiency of the apparatus.

When using the apparatus with all ports closed care must be taken to see that the oxygen flow is such that the bag does not collapse completely towards the end of inspiration. Should hyperpnœa be present the rates of flow of oxygen may require to be increased much above the figures shown in the table, until breathing becomes more normal.

TABLE VI

Oxygen flow, Litres per min. . . .	3	4	5	6	7
B.L.B. { Number of ports open . . . .	3	3	2	0	0
B.L.B. { Oxygen in alveolar air . . . .	46%	56%	69%	87%	90%
Nasal catheter, O <sub>2</sub> in alveolar air . .	27%	33%	38%	45%	..

Once the mask is adjusted the bag should fill during expiration almost to capacity, and empty during inspiration. Inadequate movement of the bag indicates either that the nose-piece is not fitting snugly or that the patient is breathing almost entirely by the mouth. This latter may be due to nasal obstruction; it is for such cases that the oronasal type is intended.

On inspiration the gas inhaled is either (a) oxygen from the bag, should all the ports be closed, or (b) a mixture of oxygen (from the bag) and of atmospheric air entering through the ports, should any be open. The atmosphere inhaled can therefore be modified by the dilution of oxygen with varying amounts of air. The accompanying table shows the alveolar oxygen concentrations at different rates of flow and with varying numbers of ports open. On expiration the bag is distended, the exhaled air first mixing with the oxygen in the bag, the excess escaping mainly by the expiratory valve.

The B.L.B. mask is suitable not only for the treatment of all types of oxygen deficiency amenable to inhalation therapy but has made possible, for the first time, the easy and economical administration of oxygen at high concentrations (95 per cent.) which hitherto have necessitated the use of such elaborate apparatus as the oxygen chamber and special tents. The possibility of attaining concentrations of oxygen of over 90 per cent. in the alveolar air extends the indications for oxygen considerably, since it is now possible to increase the normal oxygen capacity of the blood from about 19.5 vols. per cent. to approximately 22.2 vols. per cent., largely by increasing the amount carried in simple solution in the plasma.

In the peripheral circulatory failure associated with traumatic shock, and with such conditions as coronary thrombosis, a state of stagnant anoxia



exists, not affected by oxygen in moderately increased concentrations but capable of improvement to a considerable degree by the breathing of atmospheres containing oxygen in approximately 100 per cent. concentration. Its use has also been suggested as an adjunct to treatment in cases of threatened gangrene, the local anoxæmia being thereby partly relieved. Again, in carbon-monoxide poisoning the rate of elimination of the carbon monoxide is increased to four times what it is when ordinary air is breathed.

The foregoing indications depend on the enhanced oxygen-carrying power of the blood. Another series of uses depends on the fact that the nitrogen normally in solution in blood and body fluids is eliminated with moderate rapidity when oxygen is inhaled in high concentration. It can therefore be used to expedite the reabsorption of air after encephalography, to relieve gaseous abdominal distension, and subcutaneous emphysema, the gas in such cases being mainly nitrogen.

When using high concentrations of oxygen it is inadvisable to continue for more than forty-eight hours, after which time the concentration should be reduced to 60 per cent.

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## RESPIRATORS

The recent epidemic of anterior poliomyelitis justifies some consideration of the use of respirators. Although these aids to respiration have their main indication in infantile paralysis, their use is not confined to that disease. Acute polyneuritis may spread to involve respiratory mechanisms and cause severe embarrassment to breathing. Other diseases characterised by progressive weakness of muscle with inexorable deterioration to a fatal issue are better left alone when breathing becomes difficult. Indeed, some cases of anterior poliomyelitis, condemned to a life of immobility in an iron lung, long for the release of death. Unfortunately, when indications for the use of a respirator arise in anterior poliomyelitis, prognosis is never certain enough to justify the withholding of artificial aid.

When respiration is failing, the patient may be kept alive by several methods. Two principles are involved: air may be forced out of the chest by compressing the thorax or drawn into the lungs by submitting the chest and abdomen to diminished atmospheric pressure; in the former, the elasticity of the chest wall restores its natural contours when compression is released for inspiration; in the latter, expiration occurs when suction stops. Artificial respiration manually given and pulsators of the Bragg-Paul type depend on the first principle and respirators of the Drinker and Both-Nuffield type (Fig. 40) on the second. The advantages of the suction method are that respiratory exchanges are greater and normal respiration is more closely imitated. The availability of respirators—made possible through the generosity of Lord Nuffield—renders their use almost universal throughout this country. Only the Nuffield respirator will be described, as the Bragg-Paul pulsator is simple in construction and its method of use is easily grasped.

The following are the indications and advantages of the pulsator. It is better suited to children, who may accept it without that terror which the box respirator may cause. In diphtheria, the incomplete paralysis may permit the patient to fight against the iron lung and thus more harm than

good may result. Finally, the pulsator has the advantage of allowing concurrent physiotherapy.

The respirator may become necessary because of involvement of lower cranial nerves, especially the 10th, the respiratory centre and the cervico-thoracic cord. The main signs are difficulty in swallowing; anoxia and cyanosis. These signs are accompanied by weakness of the voice; sometimes in tones scarcely audible the patient will ask for help with breathing. If the breathing deteriorates rapidly, manual artificial respiration may be required while the respirator is being prepared. The accompanying illustration of the respirator is sufficiently clear to make detailed description unnecessary. Of greatest importance is the fitting of the sorbo-rubber collar; unless the contact of the collar with the neck is close, the machine is inefficient. The aperture is just large enough to fit the thinnest neck; thicker

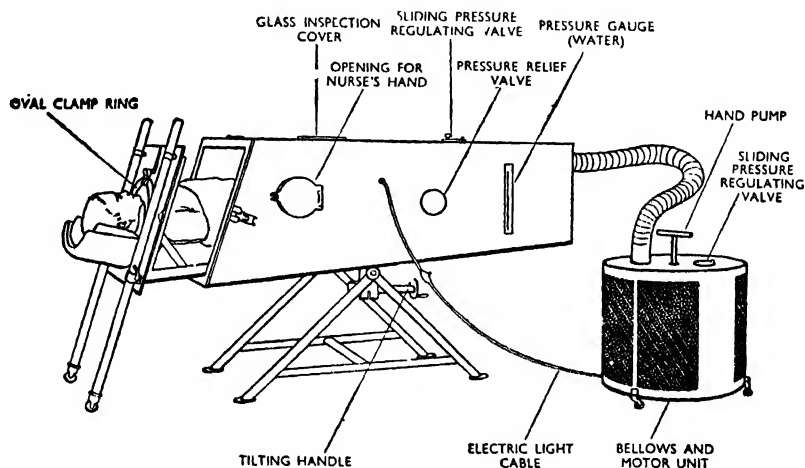


FIG. 40.—The Both-Nuffield Cabinet Respirator.

necks are accommodated by stretching the rubber and fixing it by the overlying clamping plates. The position of the neck aperture relative to the head rest is important, but can scarcely be adjusted when the patient is being put into the respirator hurriedly. After the patient has settled, the height of the aperture is adjusted; if it is too high the back of the neck will ulcerate. Cotton-wool should separate the skin from the actual rubber of the collar. When the patient has been wheeled into the respirator and the box has been made air-tight by the four clamps at the head end of the carriage, padding is placed between the shoulders and the removable end of the "lung"; the whole box is then tilted to 30° head down from the horizontal so that mucus will collect in the nasopharynx. From the nasopharynx the mucus can be easily extracted by the usual mucus extractor of the anæsthetist. Nausea and a tendency to vomit in bulbar cases may demand emptying the stomach. This can be done by passing a stomach tube after the patient has been tilted. Once the patient is in the respirator he usually settles down quickly and is soon content to let the apparatus do its work without resisting the rhythm of the pump by his own breathing effort. He scarcely needs any instruction in timing his attempts at speaking to coincide with the phases of passive expiration. A spare motor and bellows

should always be available because the motor may seize and, after some time, the rubber of the bellows will perish at its waist.

**Regulation of Depth and Frequency of Respiration.**—The gauge at the side of the respirator should be filled with water up to the zero mark before operating the apparatus. Two valves, one on the top of the box and the other on the top of the bellows, are adjusted until the water gauge reads 16 to 18 mm. water pressure at each stroke of the pump. An alteration in the frequency may be made by changing the position of the driving belt on the flanged wheels beside the motor. For most cases the rate of respiration should be that of a normal person at rest. It may be necessary to increase the rate if a pulmonary infection complicates the picture.

**Management of the Patient.**—Two principles must govern the care of the patient: first, adequate oxygenation of the blood must be ensured, and hence administration of oxygen may be helpful; secondly, recent American experience would suggest that the maintenance of a clear air-way is greatly enhanced if an elective tracheotomy has been performed. For the latter procedure there are two indications—pooling of saliva, with difficulty in swallowing, and paralysis of the larynx, which is often of the abductor type. The justification for such an extreme measure is that certain bulbar forms of poliomyelitis have a good ultimate prognosis when little or no limb paralysis is present.

Anyone attending to a patient in an iron lung should be masked, gowned and gloved. If the attendant is unmasked the patient may catch a respiratory infection; if ungloved, there is danger from infective excreta. How much the patient should be wheeled out of the lung is a matter of nursing discretion. The alarm of many when taken out may mean sacrifice of some minor service or a makeshift procedure through the portholes. In the early stages of the iron-lung life, the patient is a prey to the danger of pulmonary or other infection. With good reason a course of penicillin can be given prophylactically. The bed-pan should be of the rubber air-ring type. The usual rules are observed in giving scrupulous care to the skin (see p. 3). Loss of tissue over the anterior superior iliac spines may be so profound as to render the overlying skin particularly vulnerable in anterior poliomyelitis. Pressure from the lightest covering may break the skin; this disaster may be prevented by the use of suitable cotton-wool ring pads. Regular catheterization may be necessary: for this purpose the patient is wheeled out merely for the introduction of the catheter; the bladder is voided when the patient has been returned to the lung; suprapubic pressure may be applied through the porthole. If respiratory exchanges are so poor as to cause distress when the patient is out for attention to skin, bladder or bowel, artificial respiration may be given. Careful observation of body temperature, particularly in the early stages of the iron-lung treatment, is essential because of the danger of hyperthermia. Not only is the physiological mechanism for the control of body temperature seriously disturbed in the early stages of poliomyelitis, but the physical conditions of confinement in an iron lung are prejudicial to thermal regulation. Too often the patient has an excess of coverings. The limited cubic capacity of the "lung" limits heat loss; with a rising temperature the skin should be exposed and the valve on the top of the lung used in preference to that over the pump.

When recovery is taking place the patient should be weaned from the

respirator. This process is frequently distressing to the patient, who has come to rely on artificial aid to breathing. The length of time out of the respirator must never be so long as to cause the patient distress. Often the Bragg-Paul pulsator can be used if it is desired to have the recovering patient permanently free of the respirator for frequent physiotherapy.

A final word must be said about the attitude of the nurse or doctor in charge. The plight of respiratory paralysis is usually sufficient to guarantee sympathetic handling on the part of attendants. Sometimes terror is regarded as of functional origin and is the cause of a hardening of attitude towards the patient. Forcing a discipline in the name of superior knowledge is not only distressing to the patient but is often based on a false premise. No nurse has any subjective knowledge of the patient's problem, and, in any case, the sick-room is no place for omniscience on either side.

J. B. GAYLOR.

1

## CONVERSION TABLE FOR WEIGHTS AND MEASURES

1 Milligram (mg.)	= 0.015 gr.
1 Gramme (gm.)	= 15.4 „
1 Gramme	= 0.25 dr.
1 Gramme	= 0.03 oz.
1 Kilogram (kg.)	= 2.2 lb.
1 Kilogram	= 0.16 st.

1 Grain (gr.)	= 64.8 mg.
1 Grain	= 0.06 gm.
1 Drachm (dr.)=60 gr.	= 3.9 „
1 Ounce (oz.)=8 dr.	= 28.35 „
1 Pound (lb.)=16 oz.	= 0.45 kg.
1 Stone (st.)=14 lb.	= 6.35 „

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1 Cubic centimetre (c.c.)	= 16.9 min.
1 Cubic centimetre	= 0.28 fl. dr.
1 Cubic centimetre	= 0.035 fl. oz.
1 Litre	= 35.2 „
1 Litre	= 1.76 pints.

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1 Minim (min.)	= 0.059 c.c.
1 Fluid drachm (fl. dr.)=60 min.	= 3.6 „
1 Fluid ounce (fl. oz.)=8 fl. dr.	= 28.4 „
1 Pint=20 fl. oz.	= 0.57 litre.
1 Pint	= 568.2 c.c.

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1 Metre (m.)	= 39.37 inches.
1 Centimetre (cm.)	= 0.39 inch.
1 Millimetre (mm.)	= 0.039 „
1 Micron ( $\mu$ )	= 0.000039 inch.
1 Inch (in.)	= 25.4 mm.

# APPENDIX

## TABLE OF OFFICIAL PREPARATIONS WITH THEIR PROPRIETARY EQUIVALENTS

- Acetarsol (B.P.)** (Acetarsones).  
**ACETYLARSAN** (May & Baker).  
**DEVEGAN** (Bayer).  
**KHAROPHEN** (Burroughs Wellcome).  
**ORARSAN** (Boots).  
**SPIROCID** (Bayer).  
**STOVAR SOL** (May & Baker).
- Acetylphenylhydrazine.**  
**NIZIN** (Burroughs Wellcome).
- Adrenaline Preparations.**  
**ADRENALIN INHALANT** (Parke, Davis).  
 Contains 1 in 1,000 in oil.  
**ADRENALIN IN OIL** (Parke, Davis). Contains 1 in 500 in oil.  
**ADRENUTOL** (Evans). Contains 1 in 500 in water-glycerin.  
**HYPOLOID ADRENALINE** (Burroughs Wellcome). Contains 1 in 1,000 in aqueous solution.  
**SUPRARENALIN** (Armour). Contains 1 in 1,000.  
**VASO-CONSTRICTINE** (Duncan, Flockhart). Contains 1 in 1,000.
- Adrenaline and Ephedrine Preparations.**  
**ADREPHINE** (Parke, Davis). Adrenaline, 0.01 per cent.; Ephedrine sulphate, 2 per cent.  
**ENDRINE** (Wyeth). Ephedrine, 0.5 per cent.  
**EPHETONIN** (Napp).  
**EPHETONOGEN** (Richter). Adrenaline hydrochloride, 0.01 per cent.; ephedrine hydrochloride, 3 per cent.  
**EPHRESOL** (Evans). Ephedrine hydrochloride, 2 per cent.; adrenaline, 0.01 per cent.  
**EPINALIN** (Burroughs Wellcome). Adrenaline, 0.01 per cent.; ephedrine sulphate, 2 per cent.  
**GENOSAL** (Genatosan). Ephedrine hydrochloride 0.5 per cent.
- Adrenaline and Pituitary Preparations.**  
**EVATMINE** (British Organotherapy).  
**INFUNDRENALIN** (Evans).  
**KADAMYSIN** (Zimmerman).  
**PITRENALIN** (Parke, Davis).
- Aluminium Hydroxide (B.P.).**  
**ALOCOL** (Wander).  
**ALUDROX** (Wyeth).  
**COLLUMINA** (Evans).  
**LACTALUMINA** (Crookes).
- Amethocaine Hydrochloride (B.P.).**  
**ANETHAINE** (Glaxo).  
**DECICAIN** (Bayer).  
**PONTOCAINE** (Winthrop, New York).  
**REGIONAL D.** (Duncan, Flockhart).
- Amidopyrine (B.P.).**  
**PYRAMIDON** (Bayer).
- Aminacrine Hydrochloride (B.P.).**  
**ACRAMINE** (Glaxo).  
**DERMACRINE** (Bayer).  
**FLAVOGEL** (Glaxo).
- Aminophylline.** See Theophylline and Ethylene Diamine).
- Amphetamine (B.P.).**  
**ALLODENE** (Bush).  
**BENZEDRINE** (Menley & James).  
**DEXEDRINE** (Menley & James).  
**KARSODRINE** (Griffiths Hughes).  
**METHEDRINE** (Burroughs Wellcome).
- Amylobarbitone (B.P.C.).**  
**AMYTAL** (Lilly).
- Aneurine Hydrochloride (B.P.).** See Vitamin B<sub>1</sub>.
- Antihistamine Drugs.**  
**ANTERGAN** (May & Baker).  
**ANTHISAN** (May & Baker).  
**ANTISTIN** (Ciba).  
**BENADRYL** (Parke, Davis).  
**THENYLENE** (Abbott).  
**TORANTIL** (Bayer).
- Antimony Compounds.**  
**ANTHIOMALINE** (Lithium Antimony Thiomalate) (May & Baker).  
**NEOSTAM** (Burroughs Wellcome).  
**STILBAMIDINE** (May & Baker).
- Arsphenamine (B.P.C.).**  
**SALVARSAN** (Bayer).  
**STABILARSAN** (Boots). A stable solution in glucose.
- Ascorbic Acid (B.P.).** See Vitamin C.
- Atropine Methylnitrate.**  
**EUMYDRIN** (Bayer).  
**PYLOSTROPIN LAMELLÆ** (Clay & Abraham).
- Barbitone (B.P.).**  
**VERONAL** (Bayer).
- Barbitone Sodium (B.P.).**  
**EMBINAL** (May & Baker).  
**MEDINAL** (British Schering).  
**VERONAL-SODIUM** (Bayer).
- Barbitone and Amidopyrine, Tab. (B.P.C.).**  
**VERAMON** (British Schering).  
**VEROPYRON** (Richter).
- Benzocaine (B.P.).**  
**ANÆSTHESIN** (Bayer).  
**CYCLOFORM OINTMENT** (Bayer).
- Benzyl Benzoate (B.P.).**  
**ASCABIOL** (May & Baker).  
**BENZEVAN** (Evans).  
**PROSCABIN** (Bayer).  
**SARCOPTAN** (Duncan, Flockhart).  
**SCOBENZOL** (Boots).

**Bismuth, Inj. (B.P.).**

- BISANTOL (May & Baker).
- BISGLUCOL (May & Baker).
- BISMECOL (May & Baker).
- BISMOSTAB (Boots).
- BISMUTH ET SODII TARTRATE (B.P.) S.B.T. (Hewlett).
- CHLOROSTAB (Boots).
- "HYPOLOID" BISMUTH METAL (Burroughs Wellcome).
- "HYPOLOID" BISMUTH OXYCHLORIDE (B.P.) (Burroughs Wellcome).
- SOBITA (Howards).

**Bromethol (B.P.).**

- AVERTIN (Bayer).

**Butobarbital.**

- SONALGIN (with PHENACETIN) (May & Baker).
- SONERYL (May & Baker).

**Calciferol (B.P.).** See **Vitamin D.****Calcium Aspirin.**

- ALASIL (Wander).
- CALENO (Eno).
- CALSPRATE (Genatosan Ltd.).

**Calcium Gluconate (B.P.).**

- CALCIUM SANDOZ (Sandoz).

**Calcium Iodoxybenzoate.**

- ARTHRYTIN (May & Baker).
- CALSIOD (Menley & James).

**Calcium Lævulate (B.P.C.).**

- "HYPOLOID" CALCIUM LÆVULATE (Burroughs Wellcome).

**Carbachol (B.P.).**

- ACETYLCHOLINE (Roche).
- AMECHOL (Savory & Moore).
- CHORYL (Pharmaceutical Products).
- DORYL (Merck).
- MEOCHOLYL (Merck; Savory & Moore).
- MORYL (Savory & Moore).

**Carbromal (B.P.C.).**

- ADALIN (Bayer).
- PLANADALIN (May & Baker).

**Cataplasma Kaolini (Kaolin Poultrice) (B.P.).**

- ANTIPHLOGISTINE (Denver Chemical Co.).
- ANTITHERMOGEN (Hewlett).
- CALOPLAST (Allen & Hanburys).
- THERMOFUGE (Parke, Davis).

**Chiniofon (B.P.).**

- QUINOXYL (Burroughs Wellcome).
- YATREN (Bayer).

**Chloroxylenol (B.P.).**

- Official preparation is Liq. Chloroxylenolis (B.P.) (Roxenol) which contains 5 per cent. A powerful antiseptic, chloroxylenol or halogen derivatives of xylenol are components of the following proprietary antiseptics:—

- DETTOL (Reckitt).
- LYSANTOL (Allen & Hanburys).
- NEO-MONSOL (Monsol Ltd.).
- OSYL (Lysol Ltd.).
- ZANT (Evans).

**Cinchocaine Hydrochloride (B.P.).**

- NUPEACINE (Ciba).

**Cinchophen (B.P.).**

- AGOTAN (Howards).
- ATOPHAN (British Schering).
- TOPHOSAN (Richter).

**Citrated Ferrous Chloride (B.P.C.).**

- FERRONYL (Napp). Contains 0.05 gm. of ferrous chloride.

**Codeine Compound Tab. (B.P.).**

- VEGANIN (Warner).

**Colloidal Kaolin.**

- CARBOKAYLENE (Kaylene Ltd.). Colloidal kaolin with activated charcoal.
- CHARKAOLIN (Allen & Hanburys). Colloidal kaolin and activated charcoal.
- KAYLENE-OL (Kaylene Ltd.). Kaolin and liquid paraffin.
- LACTO-KAOLIN (Crookes).

**Curare (Tubocurarine).**

- TUBARINE (Burroughs Wellcome).
- dextro-TUBOCURARINE (Duncan, Flockhart).

**Cyclobarbitone.**

- PHANODORM (Bayer).

**Desiccated Stomach.**

- ERYTHROID (Oxo).
- EUGASTROL (Allen & Hanburys).
- EXTOMAK (Benger).
- GASTER SICCATA (British Drug Houses).
- GASTREXO (Evans).
- PEPSAC (Boots).
- VENTRÆMON (Organon).
- VENTRICULIN (Parke, Davis).
- VENTRON (Parke, Davis).

**Desoxycorticosterone Acetate (B.P.).**

- CORTENIL (Bayer).
- CORTIGEN (Richter).
- CORTIRON (British Schering).
- D.O.C.A. (Organon). Also implants.
- PERCORTEN (Ciba).
- SYNCORTYL (Roussel).

**Dichlor-Diphenyl-Trichlorethane.**

- D.D.T. (See p. 277).
- D.M.P. (DIMETHYLPHTHALATE) (Duncan, Flockhart).
- GAMMEXANE (BENZENE HEXACHLORIDE) (I.C.I.).

**Dicoumarol (B.P.).**

- COUMARIN (Herts Pharmaceuticals).
- DICOUMARIN (Organon).
- DICOUMARIN (Ward, Blenkinsop).

**Digitalis.** (See p. 637).**Diodone, Inj. (B.P.).**

- PER-ABRODIL (Bayer).
- PYELOSIL (Glaxo).
- PYLUMBRIN (Boots).
- URIODONE (May & Baker).

**Diphenan (B.P.).**

- BUTOLAN (Bayer).
- OXYLAN (Burroughs Wellcome).

**Dithranol (B.P.).**

- ANTHRALIN (Abbott).
- CIGNOLIN (Bayer).
- DEBOBIN (Glaxo).

**Emulsio Paraffin Liq. (B.P.).**

AGAROL (Warner).  
PETROLAGAR (Wyeth).

**Ergometrine Maleate (B.P.).****Ergotamine Tartrate (B.P.).**

FEMERGIN (Sandoz).  
NEO-FEMERGIN (Sandoz). This contains  
0.125 mg. of ergometrine and 0.25 mg.  
of ergotamine tartrate per tablet.

**Ethanolamine Oleate (B.P.).**

ETALATE (Parke, Davis).  
ETHAMOLIN (Glaxo).  
NEO-VARIGAIN (May & Baker).  
THANOMIN (Burroughs Wellcome).  
VARISTAB (Boots).

**Ether Vinyl (B.P.).**

VINESTHENE (May & Baker).

**Ethisterone (Pregneninolone) (B.P.).**

PROGESTORAL (Organon).

**Ethyl Chaulmoograte (Esters of Hydnocarpus Oil) (B.P.).**

ALEPOL SODIUM HYDNOCARPATE (Burroughs Wellcome).  
MOOGROL (Burroughs Wellcome).

**Ferri Sulphat. (B.P.).**

EMPLET FERROUS SULPHATE (Parke, Davis).  
Enteric coated.  
FEROSAN (Boots).  
FERSOLATE (Glaxo). Contains added  
copper and manganese.  
PLASTULES, with YEAST (Wyeth).

**Folic Acid.**

FOLIC ACID with IRON (Abbott).  
FOLVITE (Lederle, New York).  
FOLVRON with IRON (Lederle).

**Inj. Sodii Aurothiomalate (B.P.).**

AUROBIN (Richter).  
CRISALBINE (May & Baker).  
NOVACRYLIN AND OLEO-NOVACRYLIN  
(Napp).

**Other Proprietary Gold Compounds :**

MYOCRISIN (May & Baker). Sodium aurothiomalate in aqueous solution or oil suspension.  
PARMANIL (Bayer). Oily suspension of methyl glucamide of aurothioglycolic acid.  
SOLGANAL (British Schering). Water soluble. Disodium salt of 4-sulpho-methyl-amino-2-auromercaptobenzol-1-sulphonic acid.  
SOLGANAL B AND SOLGANAL B OLEOSUM are a solution and an oily suspension of aurothioglucose respectively.

**Gonadotrophic Hormones.****Anterior Pituitary Hormone :**

AMBINON (Organon). This preparation also contains the thyrotrophic factor.  
GONADOTRAPHON (Paines & Byrne).  
PRELOBAN (Bayer).

**Gonadotrophic Hormones (contd.).****Chorionic Hormone : (B.P.) Injection.**

ANTOXYLIN S (Oxo).  
ANTUTRIN S (Parke, Davis).  
ATREGONE (Abbott).  
GONADOTRAPHON S (Paines & Byrne).  
GONAN (British Drug Houses).  
PHYSOSTAB (Boots).  
PREGNYL (Organon).  
PROLAN (Bayer).

**Serum Hormone : (B.P.) Injection.**

ANTOSTAB (Boots).  
GESTYL (Organon).  
GONADYL (Roussel).  
SEROGAN (British Drug Houses).

**Anterior Pituitary and Chorionic Hormone :**

AMBINON A+PITUITARY GONADOTROPHIC HORMONE+500 I.U. CHORIONIC GONADOTROPHIC HORMONE (Organon).  
SYNAPODIN (Parke, Davis).

**Heparin (B.P.).**

DICOUMARIN (Ward, Blenkinsop).  
DICOUMARIN-SODIUM (Organon).  
HEPARIN (Boots).  
HEPARIN (Evans).  
LIQUEMIN (Roche).  
TEMPARIN (Horts Pharmaceuticals).

**Hexamine (B.P.C.).**

METHENAMINE (U.S.P.).  
METRAMINE (Oppenheimer).  
UROTROPINE (British Schering).  
VESALVINE (Martindale).

**Hexazole.**

AZOSOL (Boots).

**Hexobarbitone (B.P.).**

CYCLONAL (May & Baker).  
EVIPAN, AND SOLUBLE (Bayer).  
HEXANASTAB ORAL (Boots).

**Hexobarbitone Sodium (B.P.).**

CYCLONAL SODIUM (May & Baker).  
EVIPAN SOLUBLE (Bayer).  
HEXANASTAB (Boots).

**Hexyl-Resorcinol (B.P.C.).**

CAPROKOL (Sharp & Dohme).  
S.T. 37 (Sharp & Dohme).

**Hormone Implants.**

DESONXYCORTICOSTERONE ACETATE.  
ESTRADOL.  
PROGESTERONE.  
TESTOSTERONE PROPIONATE.  
(British Drug Houses, Roussel).

**Iodised Oil (B.P.).**

IODATOL (British Drug Houses).  
IODINOL (Martindale).  
LIPIODOL (Bengué).  
NEO-HYDRIOL (May & Baker).  
SKIADIN (Ward, Blenkinsop).

**Iodoxyl (B.P.).**

PYELECTAN (Glaxo).  
UROPAQ (May & Baker).  
UROSELECTAN B (British Schering).  
URUMBIN (Boots).

**Lauryl Thiocyanate.**

LETHANE (Ministry of Health).  
LORICIDE IMPERIAL CHEMICAL (Pharmaceuticals).



**Leptazol (B.P.).**

AZOL (Boots).  
CARDIAZOL (Knoll).  
PHRENAZOL (Boots).

**Liver Preparations for Injection.**

ANALÆMIN (British Drug Houses).  
ANA-HEPOL (Allen & Hanburys).  
CAMPOLON (Bayer).  
EXAMEN (Glaxo).  
HEMEX (Paines & Byrne).  
HEPARGLANDOL-B (Roche).  
HEPARMONE (Lilly).  
HEPASTAB (Boots).  
HEPATEX AND NEO-HEPATEX (Evans).  
HEPOLON (Allen & Hanburys).  
JECTÆMIA (Sharp & Dohme).  
PERNÆMON (Organon).  
PLEXAN (Glaxo).  
PRÆTHRON (Armour).  
RETICULOGEN (Lilly).

**Magnesium Trisilicate (B.P.).**

GASTOMAG (Boots).  
GELUSIL (Warner).  
MAGNESIL (Duncan, Flockhart).  
MAGSORBENT (Kaylene Ltd.).  
MINTOSIL (T. & H. Smith).  
NOVASORB (Evans).  
TRINESIUM (Abbott).

**Mandelic Acid (B.P.).** See p. 794.

ACIGEN (May & Baker).  
AMMOKET (Boots).  
CALCIUM MANDELATE (Burroughs Wellcome).  
HEXA-MANDELATE (Southon Laboratories).  
KETUREX (Evans).  
MANDELIC ACID ELIXIR (Lilly).  
MANDELIX (British Drug Houses).

**Menaphthone (B.P.).** See Vitamin K.**Mepacrine Hydrochloride (B.P.).**

ATEBRIN (Bayer).  
QUINACRINE (May & Baker).

**Mepacrine Methanesulphonate (B.P.).**

ATEBRIN MUSONAT (Bayer).  
QUINACRINE SOLUBLE (May & Baker).

**Mersalyl (B.P.).**

HYPOLOID MERSALYL (Burroughs Wellcome).  
NEPTAL (May & Baker) is a related mercurial diuretic.  
NOVURIT (Martindale).  
SALYRGAN (Bayer).

**Mesulphen (B.P.C.).**

MITIGAL (Bayer).  
SUDERMO (Burroughs Wellcome).

**Methyltestosterone (B.P.).**

NEO-HOMBREOL M. (Organon).  
ORAVIRON (British Schering).

**Methylthiouracil (B.P.) and Tabellæ (50 mg.).****Neocarsphenamine (B.P.).**

EVARSAN (Evans).  
NEOKHARSIVAN (Burroughs Wellcome).  
NEOSALVARSAN (Bayer).  
NOVARSAN (Allen & Hanburys).  
NOVARSENOBILLON, N.A.B. (May & Baker).  
NOVOSTAB (Boots).

**Nicotinic Acid (B.P.) and Amide.**

PELONTIN (Glaxo).

**Nikethamide (B.P.).**

ANACARDONE (British Drug Houses).  
CORAMINE (Ciba).  
CORVOTONE (Boots).  
CYCLITON (Roche).  
NICAMIDE (Burroughs Wellcome).

**Estrogenic Hormones.***Natural Estrogens :*

BENZTRONE (Paines & Byrne).  
DIMENFORMON (Organon).  
GYNCESTROL (Roussel).  
ESTRADIOL BENZOATE (Burroughs Wellcome).  
ESTRIN (Oxo).  
ESTROFORM (British Drug Houses).  
OVOCYCLIN AND OVOCYCLIN P (Ciba).  
PROGYNON B OLEOSUM FORTE (British Schering).  
THEELIN (Parke, Davis).  
UNDEN (Bayer).

*Synthetic Estrogens :*

CLINGESTROL (Glaxo).  
DIENCESTROL (Boots, British Drug Houses, Glaxo, Organon, Paines & Byrne).  
HEXCESTROL (Burroughs Wellcome, Organon, Oxo).  
MENOPAX (Clinical Products)+CALCIUM LACTATE.  
OVENDOSYN (Menley & James).  
PABESTROL AND PABESTROL D (Paines & Byrne).  
STILBESTROL (Allen & Hanburys, Bayer, Boots, Burroughs Wellcome, Organon, Oxo).  
STILBESTROL DIPROPIONATE (Bayer, Burroughs Wellcome, Glaxo, Organon).  
SYNTESTRIN (Richter).  
SYNTHOVO (Boots).

**Orthocain (B.P.).**

ORTHOFORM (Bayer).

**Oxyphenarsine Hydrochloride.**

MAPHARSEN (Parke, Davis).  
NEO-HALARSINE (May & Baker).

**Pamaquin (B.P.).**

PLASMOQUINE, PLASMOCHIN (Bayer).  
PRAEQUINE (May & Baker).

**Pancreatin, Tab. (B.P.).**

DIPANKRIN (Richter).  
FESTAN (Bayer).  
PANACOIDS (Reed & Carnrick).  
PANLITTOL (Armour).  
PANTERIC TABLETS (Parke, Davis).  
ZYMINE (Burroughs Wellcome).

**Papaveretum (B.P.C.).**

ALOPON (Allen & Hanburys).  
OMNOPON (Roche Products).  
OPIOLOID (Richter).  
OPODINE (Macfarlan).  
PAVOPIN (T. & H. Smith).

**Parathyroid Extract (B.P.C.).**

EUPARATONE (Allen & Hanburys).  
PARATHORMONE (Lilly).  
PARATHYROID COMPOUND (Armour).  
PAROIDIN (Parke, Davis).

**Penicillin (B.P.).***Official Preparations :*

- CREMOR PENICILLINI (500 I.U. per gm.).  
 CREMOR PENICILLINI STERILISATUS (500 I.U. per gm.).  
 INJECTIO PENICILLINI (50,000 units per ml.).  
 INJECTIO PENICILLINI OLÉOSA (I.M.) (125,000 units per ml.).  
 OCULENTUM PENICILLINI (1,000 units per gm.).  
 TROCHISCI PENICILLINI (500 units in each).  
 UNGUENTUM PENICILLINI (500 units per gm.).

*Proprietary Preparations :*

- PENEUCIN (PENICILLIN OINTMENT B.P.) (Herts Pharmaceuticals).  
 Auracones, each 500 I.U. (Duncan, Flockhart).  
 Dental Cones, each 5,000 I.U. of the calcium salt with sulphathiazole, gr.  $\frac{1}{2}$ , and sulphanilamide, gr.  $\frac{1}{2}$  (May & Baker).  
 Pessaries, each 5,000 units in cocoa-butter (Camden Chemical Co.).  
 Solution Tablets (Allen & Hanburys, Burroughs Wellcome).

**Pentobarbitone Sodium (B.P.).**

NEMBUTAL (Abbott).

**Pentose Nucleotide, Liq.**

- PENTIDE (Allen & Hanburys).  
 PENTNUCLEOTIDE (Menley & James).  
 S.P.N. (Evans).

**Pethidine Hydrochloride (B.P.).**

- DEMEROL, ISONIPECAINE (in U.S.A.).  
 DOTANTAL (Bayer).

**Pemitone (Methylphenobarbitone) (B.P.).**

PROMINAL (Bayer).

**Phenobarbitone (B.P.).**

- GARDENAL (May & Baker).  
 LUMINAL (Bayer).  
 SOMONAL (Richter).

**Phenytoin Soluble (B.P.).**

- DILANTIN SODIUM, EPANUTIN (Parke, Davis).  
 EPTOIN (Boots).  
 HYDANTAL (Burroughs Wellcome).  
 SOLANTOIN (Glaxo).

**Pholedrine (B.P.C.).**

- PHOLETONE (Boots).  
 STIMATONE (Ward, Blenkinsop).  
 VERITOL (Knoll).

**Pbthylsulphathiazole (B.P.C.).**

- SULPHATHALIDINE (Sharp & Dohme).  
 THALAZOLE (May & Baker).  
 THALISTATIN (Herts Pharmaceuticals).

**Pituitary Extract, Liq. (B.P.).**

- GLANDUTRIN (Richter).  
 HYPOPHYSIN (Bayer).  
 INFUNDIBULIN (Evans).  
 INFUNDIN (Burroughs Wellcome).  
 PITIBULIN (Allen & Hanburys).  
 PITON (Organon).  
 PITOXYLIN (Oxo).  
 PITRESSIN (Parke, Davis).  
 PITUITRIN (Parke, Davis).

**Procaine Hydrochloride (B.P.).**

- NOVOCAIN (Bayer).  
 NOVOCAINE (Saccharin Corporation).  
 PARSETIC (Parke, Davis).  
 PLANOCAINE (May & Baker).  
 SEVICAIN (Glaxo).

**Procaine and Adrenaline Injection (B.P.).**

- ARECAN (Evans).  
 ASENSITINE (Duncan, Flockhart).  
 DURACAIN (Procaine Benzoate) (May & Baker).  
 NOVUTOX (Pharmaceutical Mfg. Co.).  
 SPINOCAIN (Bayer).

**Progesterone (B.P.).***Intramuscular Administration :*

- GESTONE (Paines & Byrne).  
 LIPO-LUTIN (Parke, Davis).  
 LUTEOSTAB (Boots).  
 LUTOCYCLIN (Ciba).  
 LUTOGYL (Roussel).  
 LUTREN (Bayer).  
 PROGESTERONE (Burroughs Wellcome, Oxo).  
 PROGESTIN (British Drug Houses, Organon).  
 PROLUTON (British Schering).

*Oral Administration :*

- ETHISTERONE (British Drug Houses, Boots).  
 GESTONE (Paines & Byrne).  
 LUTOCYCLIN LINGUETS (Ciba).  
 LUTOGYL (Roussel).  
 PROGESTORAL (Organon).  
 PROLUTON C (British Schering).

**Prolactin.**

- PROLACTIN (Allen & Hanburys).  
 PHYSOLACTIN (Glaxo).  
 RUTIN (Abbott; Allen & Hanbury).

**Salt Substitutes (Chloride free).**

- RUTHMOL (Antigen).  
 SELAROM (Bayer).

**Silver Protein (B.P.).**

PROTARGOL (Bayer).

**Silver Protein, Mild (B.P.C.).**

- ARGYROL (Barnes; Fassett & Johnson).  
 ARVITIN (Johnson).  
 CARGENTOS (Sharp & Dohme).  
 LUNARGEN (Lilly).

**Sodium Aminoarsonate (B.P.C.).**

SOAMIN (Burroughs Wellcome).

**Stibophen (B.P.).**

FOUADIN (Bayer).

**Stilbæstrol (B.P.).**

- CLINESTROL (Glaxo).  
 GYNOSONE (Imperial Chemical Pharmaceuticals).  
 OVENDOSYN (Menley & James).  
 PABESTROL (Paines & Byrne).  
 SYNTESTRIN (Richter).

**Streptomycin.**

(Distillers Co. Ltd., Glaxo).

**Succinylsulphathiazole (B.P.).**

- COLISTATIN (Herts Pharmaceuticals).  
 SULPHASUXIDINE (Sharp & Dohme).

**Sulphacetamide and Soluble (B.P.).**

ALBUOID (British Schering).

STERAMIDE (Ward, Blenkinsop).

**Sulphadiazine and Soluble (B.P.) Tabellæ and Inj.****Sulphadimethylpyrimidine (B.P.C.).**

SULPHAMEZATHINE (Imperial Chemical Pharmaceuticals).

**Sulphaguanidine (B.P.).**

GUAMIDE (Watford Chemical Co.).

**Sulphanilamide (B.P.).**

AMBESID (Richter).

COLSULANYDE (Menley &amp; James).

P.A.B.S. (Hewlett).

PRONTOSIL ALBUM (Bayer).

RUBIAZOL-A (Roussel).

STREPTOCIDE (Evans).

SULPHONAMIDE-P (Burroughs Wellcome).

**Sulpharsphenamine (B.P.)**

KHARSULPHAN (Burroughs Wellcome).

METARSENOBILLON, M.A.B. (May &amp; Baker).

MYOSALVARSAN (Bayer).

SULFARSENOL (Modern Pharmacals).

SULPHOSTAB (Boots).

**Sulphathiazole (B.P.) and Sulphathiazole Sodium (B.P.).**

CIBA 3714 (Ciba).

CIBAZOL (Ciba).

M. AND B. 760 (May &amp; Baker).

THIAZAMIDE (May &amp; Baker).

**Suprarenal Cortex Extract (B.P.C.).**

CORTIN (Organon). One c.c. equivalent to 50 gm. whole gland.

ESCHATIN (Parke, Davis). One c.c. equivalent to 40 gm. of suprarenal cortex.

EUCORTONE (Allen &amp; Hanburys). One c.c. equivalent to 75 gm. of suprarenal cortex.

SUPRACORT (Paines &amp; Byrno).

**Suramin (B.P.).**

ANTRYPOL (Imperial Chemical Pharmaceuticals).

BAYER 205; GERMANIN (Bayer).

**Testosterone (Male Hormone).**

NEOHOMBREOL (Organon).

PERANDREN (Ciba).

STERANDRYL (Roussel).

TESTOSTERONE DIPROPIONATE (Bayer, Boots, British Drug Houses, Burroughs Wellcome, Oxo).

TESTOVIRON (British Schering).

**Tetraethylthiuram.**

TETMOSOL (I.C.I.).

**Theobromine Calcium Salicylate.**

CALCIUM-DIURETIN (Knoll; Savory &amp; Moore).

THEOCALCIN (Knoll; Savory &amp; Moore).

**Theobromine and Phenobarbitone, Tab. (B.P.C.).**

THEOBA (Burroughs Wellcome).

THEOGARDENAL (May &amp; Baker).

THEOMINAL (Bayer).

**Theobromine and Sodium Salicylate (B.P.).**

DIURETIN (Knoll; Savory &amp; Moore).

**Theophylline and Ethylene Diamine (B.P.).**

CARDOPHYLLIN (Whiffen).

CARENA (Continental Laboratories).

GENOPHYLLIN (Genatosan Ltd.).

THEAMIN (THEOPHYLLINE ETHANOLAMINE) (Lilly).

**Theophylline and Sodium Acetate (B.P.).**

THEOCIN SODIUM ACETATE (Bayer).

**Thiopentone Sodium (B.P.).**

INTRAVAL SODIUM (May &amp; Baker).

KEMITHAL (Imperial Chemical Pharmaceuticals).

PENTOTHAL (Abbott).

THIOPENTONE SOLUBLE (Boots).

**Thiouracil (B.P.) and Tab. (50 mg.).****Thromboplastin.**

COAGULEN-CIBA (Ciba).

HEMAGULEN (Lilly).

HEMOPLASTIN (Parke, Davis).

THROMBIN COAGULANT (Maw).

**Thyroideum (B.P.).**

ELITYRAN (Bayer).

THYROPROTEIN (Parke, Davis).

 **$\alpha$ -Tocopheryl Acetate (B.P.C.). See Vitamin E.****Trichloroethylene (B.P.).**

TRILENE.

**Tryparsamide and Inj. (B.P.).**

HYTOLOID TRYPARSAMIDE (Burroughs Wellcome).

TRYPARSAMIDE (May &amp; Baker).

**Vitamin A.***Official Preparations:*

LIQ. VITAMIN A CONC. (B.P.), containing 50,000 I.U. of vitamin A per gramme.

LIQ. VITAMIN D CONC. (B.P.), containing 10,000 I.U. of vitamin D per gramme.

LIQ. VITAMIN A AND D CONC. (B.P.), containing 50,000 I.U. of vitamin A and 5,000 I.U. of vitamin D per gramme.

OILUM VITAMINATUM (B.P.C.), containing 1,000 I.U. of vitamin A and 100 I.U. of vitamin D per gramme.

*Proprietary Preparations:*

AVOLEUM (British Drug Houses). Contains 30,000 I.U. per gramme.

DAVITAMON A (Organon). Contains 6,000 I.U. of vitamin A per c.c. DAVITAMON A FORTE contains 60,000 I.U. per c.c.

PLANAVIT A (May &amp; Baker). Contains 25,000 I.U. per c.c.

PREPALIN (Glaxo). Contains 72,000 I.U. per c.c. Capsules each contain 24,000 I.U.; 1 c.c. ampoules each contain 100,000 I.U.

**Vitamin A and D.***Official Preparations* are given under Vitamin A.*Proprietary Preparations:*

ADEXOLIN (Glaxo). Each 3-minim capsule contains 4,500 I.U. of vitamin A and 900 I.U. of vitamin D.

DAVITAMON AD (Organon). Contains 6,000 I.U. of vitamin A and 5,000 I.U. of vitamin D per c.c.

**Vitamin A and D (contd.).**

DEKADEXOLIN (Glaxo) for intramuscular injection. Contains 60,000 I.U. of vitamin A and 10,000 I.U. of vitamin D per c.c.

HEPICOLEUM (Lilly). Capsules containing 8,500 I.U. of vitamin A and 1,700 I.U. of vitamin D.

RADIOSTOLEUM (British Drug Houses). Liquid contains 15,000 I.U. of vitamin A and 3,000 I.U. of vitamin D per gramme. Also in capsules and emulsion.

CONCENTRATED RADIOSTOLEUM for injection. Contains 75,000 I.U. of vitamin A and 15,000 I.U. of vitamin D per gramme.

**Vitamin B<sub>1</sub> (Aneurine Hydrochloride, B.P.) (Thiamin).**

BEFORTISS (Vitamins Ltd.).

BENERVA (Roche).

BERIN (Glaxo).

BETABION (Merck; Savory & Moore).

BETALIN (Lilly).

BETAXAN (Bayer).

DAVITAMON B<sub>1</sub> AND FORTE (3 mg.) (Organon Laboratories).

**Vitamin B<sub>2</sub> (Riboflavin, Lactoflavin, B.P.).**

BEFLAVIT (Roche).

MARMITE (YEAST EXTRACT).

**Vitamin B<sub>6</sub> (Pyridoxine) (Adermin).**

BENADON (Roche).

PYRIDOXINE (Crookes).

**Vitamin C (Ascorbic Acid, B.P.).** Issued in 5 mg., 25 mg. and 50 mg. tablets, and ampoules of 100 mg. and 500 mg.

CANTAN (Bayer).

CEBTONE (Merck; Savory & Moore).

CELIN and INFANT CELIN (Glaxo).

DAVITAMON C (Organon).

PLANAVIT C (May & Baker).

REDOXON (Roche).

**Vitamin D (Vitamin D<sub>2</sub>. Calciferol, B.P.).***Official Preparations :*

LIQ. CALCIFEROL (B.P.). Contains 3,000 I.U. per gramme.

LIQ. VITAMIN A AND D CONC. (B.P.). Contains 50,000 I.U. of vitamin A and 5,000 I.U. of vitamin D per gramme.

LIQ. VITAMIN D CONC. (B.P.). Contains 10,000 I.U. per gramme.

TAB. CALCIFEROL Co. (B.P.C.) or COMPOUND TABLETS OF CALCIFEROL. Contain per tablet 7½ gr. of calcium sodium lactate, 2½ gr. calcium phosphate, and 450 gr. calciferol (=500 I.U.).

*Proprietary Preparations :*

CALCIUM C. VITAMIN D (Crookes). One c.c. contains calcium 1 in 2,000, Vitamin D 5,000 I.U.

**Vitamin D (contd.).**

CALCYDOL (Allen & Hanburys). Granules containing per drachm 7½ gr. dicalcium phosphate, 1,500 I.U. of vitamin D.

CALSIMIL (British Drug Houses). Tablets containing 5 gr. calcium sodium lactate and 500 I.U. of vitamin D.

DAVITAMON D (Organon). Solution and ampoules containing 5,000 I.U. of vitamin D per c.c. DAVITAMON D FORTE contains 12,500 I.U. per c.c. DAVITAMON D SUPERFORTE contains 300,000 I.U. per c.c.

OSTELIN (Glaxo). Liquid contains 5,000 I.U. per c.c.; tablets contain calcium glycerophosphate 2 gr. and 500 I.U. vitamin D. COLLOIDAL CALCIUM WITH OSTELIN for injection contains 5,000 I.U. of vitamin D and 0.5 mg. of colloidal calcium per c.c. OSTOCALCIUM TABLETS contain 7½ gr. calcium sodium lactate, 3.6 gr. calcium phosphate, and 500 I.U. vitamin D. OSTELIN HIGH POTENCY TABLETS contain 50,000 I.U. vitamin D (Calciferol). Ampoules contain 300,000 I.U.

RADIOSTOL (British Drug Houses). A brand of liq. calciferol (B.P.). RADIOSTOL PELLETS contain 3,000 I.U. of vitamin D.

STEROGYL-15 (Roussel). Ampoules containing 600,000 I.U. in oil.

**Vitamin E (α-Tocopheryl Acetate) (B.P.).**

DAVITAMON E (Organon).

EPHYNAL (Roche). Tablets containing 3 mg. α-tocopheryl acetate.

FERTILOL (Vitamins Ltd.). Wheat germ oil in 8-minim capsules.

PHYTOFEROL (British Drug Houses). Capsules containing wheat germ oil concentrate equivalent to 6 mg. α-tocopherol.

VITEOLIN CAPSULES (Glaxo). Three-minim capsules of a wheat germ oil concentrate.

ZYGON (Squibb), TRIGOL (wheat germ oil) (Abbott) are similar preparations.

**Vitamin K.**

KLOTGEN (Abbott) is a vitamin K concentrate.

The synthetic analogue of vitamin K, 2-methyl-1 : 4 naphthoquinone, is Menaphthone (B.P.). The acetyl derivative is :

ACETOMENAPHTHONE (B.P.) or 1 : 4-diacetoxy-2-methylnaphthalene.

*Proprietary vitamin K analogues :*

DAVITAMON K (Organon).

KAPILON (Glaxo).

KAPPAXAN (Bayer).

PROKAYVIT (British Drug Houses).

SYNKAVIT (Roche).

**Vitamin P (Hesperidin).**

PERMIDIN (Glaxo). Each tablet contains 150 mg.



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